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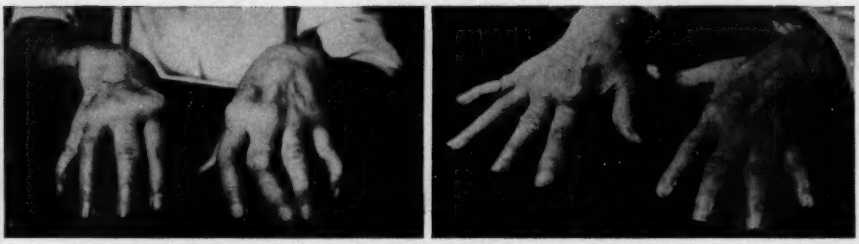

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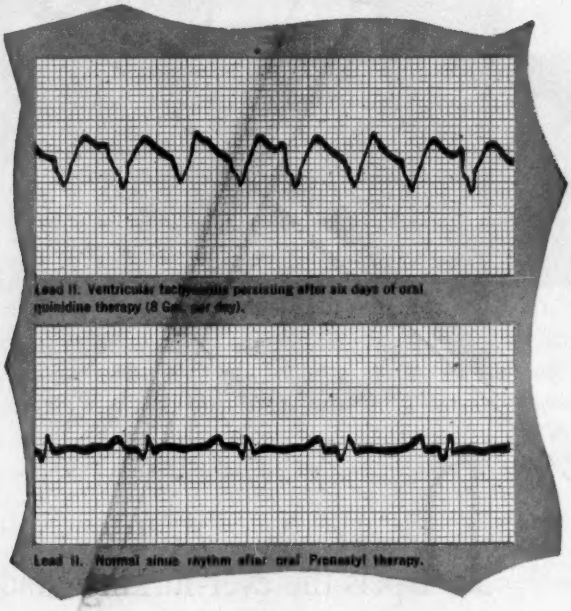

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1. Kaufman, R., and Farmer, L. (1951), Norisodrine by Aerohalor in Asthma, Ann. Allergy, 9:89, Jan.-Feb. 2. Swartz, H. (1950), Norisodrine Sulphate (25 Per Cent) Dust Inhalation in Severe Asthma, Ann. Allergy, 8:488, July-August. 3. Krasno, L., Grossman, M., and Ivy, A. (1949), The Inhalation of 1-(3',4'-Dihydroxyphenyl)-2-Isopropylaminoethanol (Norisodrine Sulfate Dust), J. Allergy, 20:111, March.


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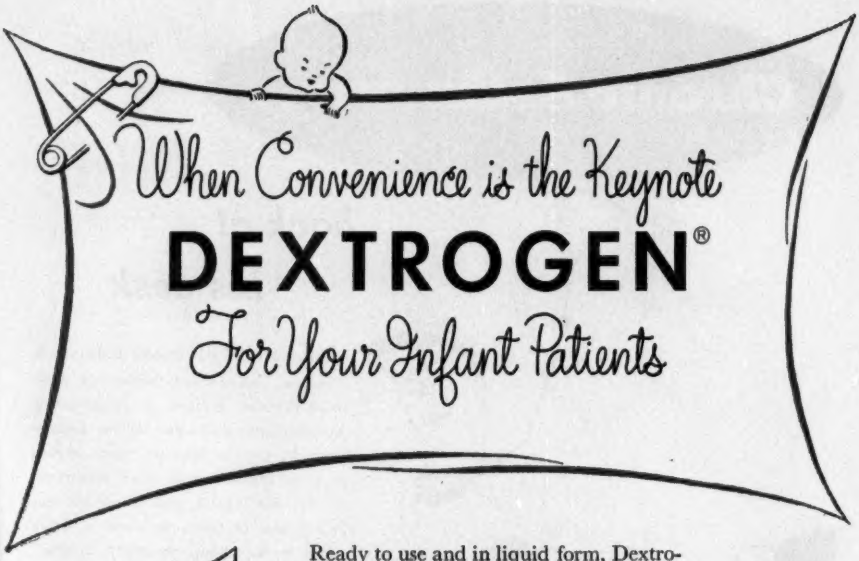

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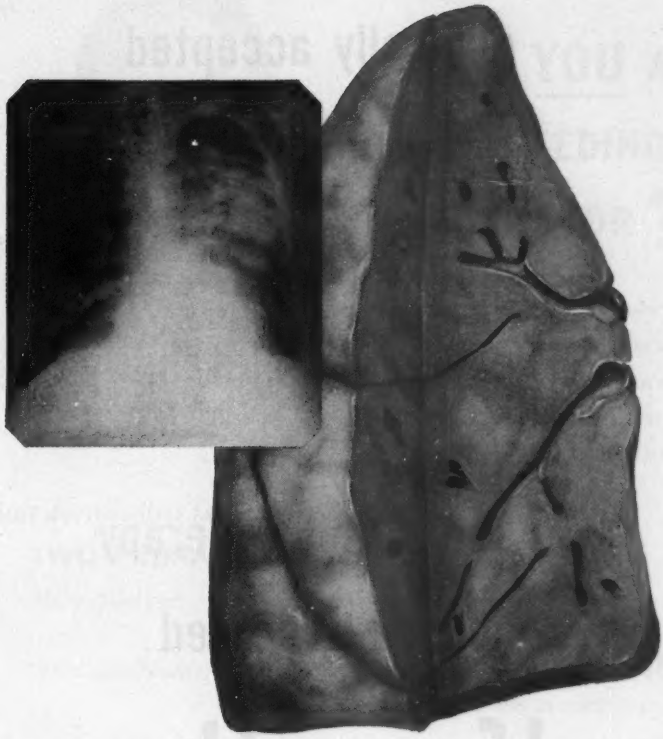

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*Potterfield, T. G., and Starkweather, G. A.: J. Philadelphia General Hosp. 2:6 (Jan.) 1951.*

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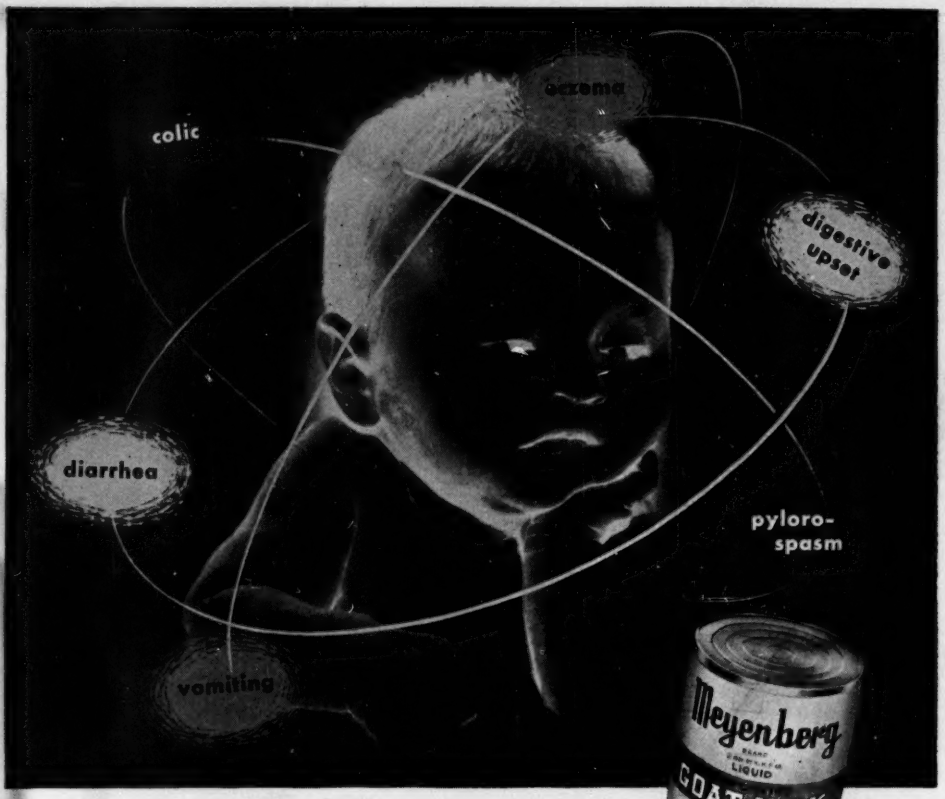


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# CONTENTS

PAGE

**Nonendocrine Deviations from the Normal Pattern of Osseous Development.** RICHARD WAGNER, M.D., BOSTON ..... 519

**Physical Changes Associated with Adolescence in Boys.** EARLE L. REYNOLDS, PH.D., AND JANET V. WINES, A.B., YELLOW SPRINGS, OHIO ..... 529

**Use of Desoxycorticosterone Acetate in Dehydration and Malnutrition in Infancy.** JOHN A. BIGLER, M.D., AND HOWARD S. TRAISMAN, M.D., CHICAGO ..... 548

**Blood Level of Thiamine in Normal Children.** HARRY A. WAISMAN, PH.D., M.D.; TONG SOO CHO, M.D.; JULIUS B. RICHMOND, M.D., AND STARKS J. WILLIAMS, M.D., CHICAGO ..... 555

**Arteriosclerosis in Infancy.** BERNARD L. LIPMAN, M.D.; IRA M. ROSENTHAL, M.D., AND HARRY LOWENBURG JR., M.D., PHILADELPHIA ..... 561

**CASE REPORTS:**

**Salmonella Meningitis: Recovery from Meningitis Due to Salmonella Sp. (Type Montevideo), with Consideration of the Problem of Salmonella Meningitis.** MARY L. BEENE, M.S.; ARILD E. HANSEN, M.D., PH.D.; GALVESTON, TEXAS, AND MACDONALD FULTON, PH.D., CHICAGO ..... 567

**Neurofibromatosis in a Newborn Infant.** BEATRICE E. SCOTT, M.D., AND HARRY J. COHEN, M.D., NEW YORK ..... 574

**Endocardial Fibroelastosis.** WILLIAM T. HILL, M.D., AND WILLIAM A. REILLY, M.D., LITTLE ROCK, ARK. ..... 579

**Adenoma of Bronchus in a Nine-Year-Old Child.** SAUL SMOLLER, M.D., AND AUBRE DE L. MAYNARD, M.D., NEW YORK ..... 587

**PROGRESS IN PEDIATRICS:**

**Causes of Congenital Defects: A Review.** F. CLARKE FRASER, PH.D., M.D., AND T. D. FAINSTAT, M.SC., MONTREAL, CANADA ..... 593

**ABSTRACTS FROM CURRENT LITERATURE** ..... 604

**NEWS AND COMMENT** ..... 654

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# NONENDOCRINE DEVIATIONS FROM THE NORMAL PATTERN OF OSSEOUS DEVELOPMENT

RICHARD WAGNER, M.D.
BOSTON

THE BONE age, as measured by the number of ossification centers which are calcified, has become an index of the stage of development of the growing child. The disturbances in the appearance of these ossification centers associated with endocrine dysfunction are clearly defined. But there are many instances of abnormal ossification in which the causative factors are not understood.

The purpose of this paper is to describe a small group of patients, some with retarded and others with precipitated development of ossification centers, who did not have other evidence of endocrine dysfunctions, and the occurrence of nonrachitic craniotabes in the latter group.

## REPORT OF CASES

The first six cases are examples of retarded osseous development (Table 1). Five of these children were short in stature, and none of the six revealed any sign of the endocrine disorders which are characterized by delayed skeletal maturation.

The next seven cases (Table 2) are examples of advanced osseous development in children who did not reveal any other signs of precipitated development, particularly no sex precocity or other evidence of an endocrine disorder. Their height did not exceed that of normal children of their age group. Five of the children had marked nonrachitic craniotabes.

## COMMENT

The 13 cases which are presented illustrate deviations from the normal pattern of development. Involvement of the skeleton is a feature in all of the cases. In Warkany and Nelson's experimental studies on rats [1] in which anomalies were produced by dietary deficiency, the skeleton was the principal site of involvement. Most of the congenital anomalies in human pathology which are known as syndromes with special names reveal characteristic abnormalities of the skeleton. Examples of such entities are Mongolism, hypertelorism, dyschondroplasia (chondrodystrophy), eccentro-osteochondrodysplasia (Morquio's disease), lipochondrodystrophy (dysostosis multiplex), acrocephalosyndactylia, primordial nanosomia, arachnodactyly, and fragilitas ossium (osteogenesis imperfecta).

---

Read before the Sixth International Congress of Pediatrics, Zurich, Switzerland, July 24 to 28, 1950.

From the Department of Pediatrics of Tufts College Medical School, the Boston Floating Hospital, and the Children's Department of the Boston Dispensary.

1. Warkany, J., and Nelson, R. C.: Anat. Rec. 79:83, 1941.

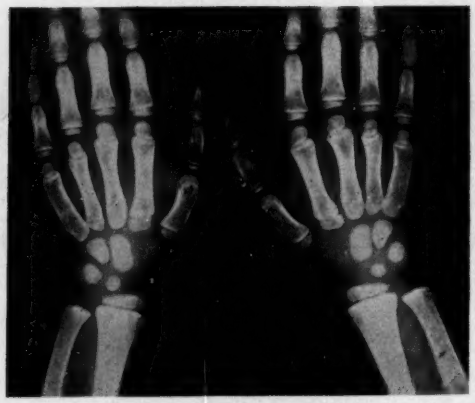

Fig. 1 (Case 1).—Retarded osseous differentiation; pseudoepiphyses on the proximal end of both second metacarpals.

Fig. 2 (Case 2).—Marked retarded osseous differentiation; asymmetric development; pseudoepiphyses on the proximal end of both second metacarpals.

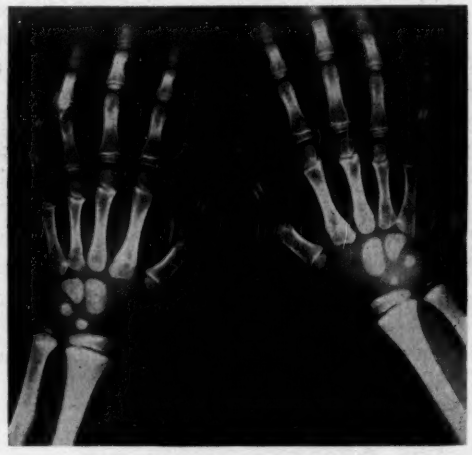

Fig. 3 (Case 3).—Marked retarded ossification; pseudoepiphyses of the metacarpals of both index fingers.

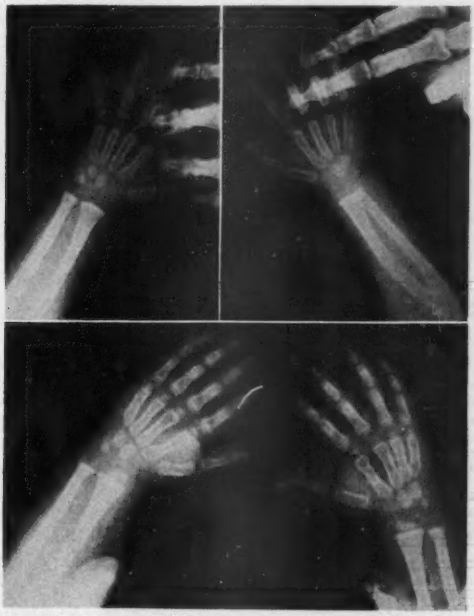

Fig. 4 (Case 4).—Above, disharmonic development; radio-ulnar synostosis; asymmetric osseous differentiation. Below, for comparison, wrists of his normally developed unidentical twin brother.

Fig. 5 (Case 5).—Retarded osseous development; bone age of a child of 2 to 3 years (patient 7 5/12 years).

Retardation in the osseous development of the wrist bones as demonstrated by roentgen examination is one of the manifestations of endocrine disturbances. However, hormones are only one of the many factors which influence growth and skeletal differentiation. Many of the well-defined syndromes with multiple congenital anomalies involving mesenchymatous structures are linked with retarded growth and development. Therefore, in the study of children with deviations from the norm of growth and osseous development, congenital malformations should be recognized. The analysis of a skeletal roentgenogram, for instance of the hand, should be used not only to compare the chronological and the bone age on the

TABLE 1.—*Patients with Retarded Osseous Development*

| Case No. | Sex | Age, Yr. | Measurements Compared with Average for Age: Height, In. | Measurements Compared with Average for Age: Weight, Lb. | Wrist Roentgenogram | Comment |
|---|---|---|---|---|---|---|
| 1 | M | 6 10/12 | 41.75/50 | 40/55 | Retarded osseous differentiation; only the capitate, hamate, triquetrum, lunate, and distal epiphysis of the radius calcified; pseudoepiphyses on the proximal end of both second metacarpals (Fig. 1) | Retarded relative growth rate; otherwise normal, doing well in school; no endocrine anomalies detectable; no response to thyroid treatment |
| 2 | M | 9 11/12 | 43/56.5 | 47/76 | Marked retardation of osseous differentiation; asymmetric development, the navicular bone being present on only one side; pseudoepiphyses on the proximal end of both second metacarpals (Fig. 2) | Has been outgrown by his younger brother; systolic murmur along the left border of the sternum with maximal intensity in third intercostal space; never cyanotic; no evidence of functional disturbance of the heart; IQ 72; basal level 6 yr. |
| 3 | M | 7 8/12 | 46.25/52.5 | ..... | Markedly retarded ossification of the carpal bones and pseudoepiphyses of the metacarpals of both index fingers (Fig. 3) | Other congenital anomalies: marked malocclusion and hypertrichosis |
| 4 | M | 2 | 30/35 | ..... | In the left wrist: capitate, hamate, and triquetrum, in the right wrist only capitate and hamate; distal epiphysis of the radius and epiphysis of the first metacarpal not yet calcified (disharmonic development); radio-ulnar synostosis, involving the proximal aspects of the bones on the right side; asymmetric osseous differentiation (no triquetrum on the side of the radio-ulnar synostosis) (Fig. 4) | Mentally alert, but always slower in development than his twin brother (not identical); first teeth at 7 mo.; can stand and take a few steps; repeats words; in Fig. 4 the wrists of the normally developed twin brother are shown for comparison |
| 5 | M | 7 5/12 | 48.25/51 | 55/59 | Only capitate, hamate, triquetrum, distal epiphysis of the radius, and epiphysis of first metacarpal calcified (bone age of a child of 2 to 3 yr.); ossification centers normal in size (Fig. 5) | On the occasion of a general examination the retarded osseous development was noted, and thyroid treatment prescribed by the family physician; repeat roentgenogram after three months showed no progress in osseous differentiation |
| 6 | M | 4 | 36.25/42.5 | 30/38.5 | Only capitate, hamate, and distal epiphysis of the radius calcified (bone age of a child of 1 yr.) | Interventricular septal defect; mother of the child exhibits a fusion of some of the vertebral bodies |

basis of the number of ossification centers which are calcified but also to determine other important details with regard to shape and formation of the structures involved and the order in which the calcification of the ossification centers takes place. This order is well-established in the anlage and follows a definite pattern. The hormones do affect the skeletal maturation, but the end organ can be affected also by the genetic or constitutional pattern of the individual.

The examples cited in this paper can be subdivided into two groups, the first characterized by retarded, the second by precipitated, bone development. All six patients of the first group are boys, five of them are markedly below the average

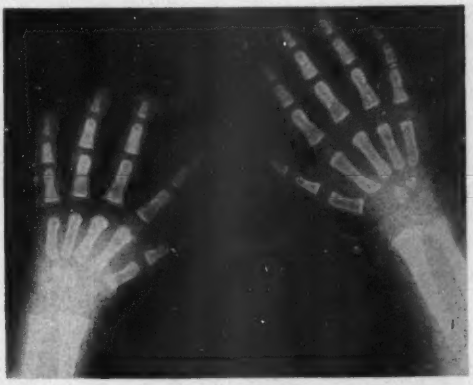

Fig. 6 (Case 7).—Advanced osseous differentiation; disharmonic development.

Fig. 7 (Case 8).—Advanced osseous differentiation; deformity of middle phalanx of both fifth fingers, as in Mongolism.

Fig. 8 (Case 9).—Advanced osseous differentiation; disharmonic development.

height of their age, while in the second group there are five girls and only two boys. It may be that the predominance of girls in the second group is an expression of the well-established fact that girls are in general ahead of boys in their development. However, the material is too small for general conclusions. Bakwin [2]

Fig. 9 (Case 12).—Strikingly advanced osseous differentiation; disharmonic development; slight asymmetry.

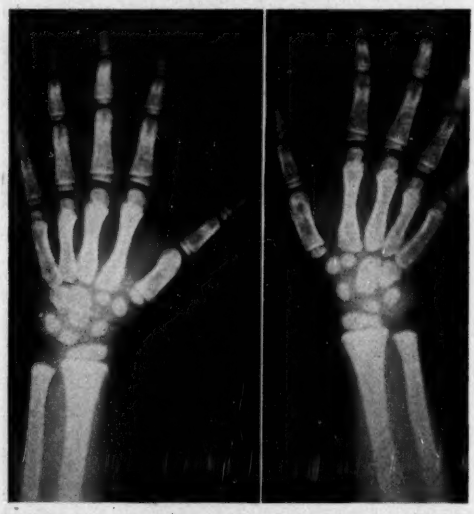

Fig. 10 (Case 13).—Ossification of all seven carpal bones on both sides and beginning ossification of the distal epiphyses of the ulna on one side.

has recently pointed out early differences in osseous development in the two sexes. He found the proximal epiphysis of the first metacarpal to be present three months and the epiphysis for the second metacarpal one year nine months earlier in girls.

2. Bakwin, H.: Personal communication to the author.

Five of the children (four of whom were girls) of the second group had nonrachitic craniotabes, and three revealed early dentition. In four of the group with minus variations other skeletal anomalies were demonstrated, in three pseudoepiphyses at the proximal ends of the second metacarpal and in one a radio-ulnar synostosis.

Pseudoepiphyses are one of the mesenchymatous stigmas, which are known to occur in some instances of multiple congenital anomalies, e. g., in Mongolism. My colleagues and I have observed them also in two children with acute lymphatic leukemia and recently in a child of 2 years with mental retardation, widening of the

TABLE 2.—*Patients with Advanced Osseous Development*

| Case No. | Sex | Age, Mo. | Wrist Roentgenogram | Comment |
|---|---|---|---|---|
| 7 | F | 3½ | No signs of rickets; osseous differentiation markedly advanced; in both wrists capitate, hamate, and triquetrum calcified, on one side even the epiphysis of the middle phalanx of the fifth finger; distal epiphysis of the radius not yet calcified (disharmonic development) (Fig. 6) | Normal growth and development; marked craniotabes; no clinical evidence of rickets; vitamin D prophylaxis since birth; blood calcium, phosphorus, and phosphatase levels within normal limits; at 5 mo. craniotabes healed; the two lower central incisors erupted |
| 8 | F | 3 | Capitate and hamate on both sides; deformity of the middle phalanx of both fifth fingers as in Mongolism (Fig. 7) | Normal growth and development; marked craniotabes; no signs of rickets; vitamin D prophylaxis since birth |
| 9 | M | 5½ | Capitate, hamate, triquetrum, and lunate on both sides; no distal epiphyses of the radius (disharmonic development) (Fig. 8) | Normal growth and development; marked craniotabes; no signs of active rickets; vitamin D prophylaxis since birth; blood calcium, phosphorus, and phosphatase levels within normal limits |
| 10 | F | 4½ | Capitate and hamate in both wrists | Normal growth and development; marked craniotabes; no signs of rickets; vitamin D prophylaxis since birth; the two lower central incisors erupted |
| 11 | F | 6 | Capitate, hamate, distal epiphysis of the radius and beginning ossification of some of the epiphyses of the phalangeal bones | Normal growth and development; marked craniotabes; no signs of rickets; vitamin D prophylaxis since birth |
| 12 | M | 7½ | Strikingly advanced osseous differentiation; six carpal ossification centers calcified: those of the capitate, hamate, triquetrum, lunate, navicular, and major multangular bone, in addition to it the distal epiphysis of the radius; the epiphysis of the first metacarpal and the distal epiphysis of the ulna not yet calcified (disharmonic development) (Fig. 9) | Normal growth and development; exhibited a peculiar anomaly of the blood picture; admitted because of question of agranulocytosis; was treated at home with diphenhydramine hydrochloride in the usual dosage for an asthmatic type of bronchitis; physical examination negative except for a slight respiratory infection and a mild pyoderma; premature eruption of the deciduous teeth (the four central incisors and the two upper lateral incisors, all six teeth of considerable size); total white-blood-cell count varied from 9,000 to 12,000 per cubic millimeter, with 1 to 7% polymorphonuclear leucocytes; bone-marrow puncture: lymphocytosis and arrest of development of the granuloeytes at the band stage |
| 13 | F | 48 | Ossification of all seven carpal bones on both sides and beginning ossification of the distal epiphysis of the ulna on one side (Fig. 10) | Admitted because of behavior difficulties and stammering; spina bifida occulta and abnormal hair growth over the lumbar region |

bridge of the nose, and prominent epicanthal folds. In the latter instance roentgenography of the skull also revealed marked flattening of the sella turcica. Pseudoepiphyses are seen only on the metacarpals of the index finger. This is probably the result of interference with the development of this bone during the prenatal period. Fusion of long bones is not an unusual skeletal anomaly in children with multiple congenital defects. Fusion of ribs or syndactylia of different grades occur either as isolated stigmas or in combination with other defects. In Cases 2 and 6 systolic murmurs and in Case 3 malocclusion and hypertrichosis were present. In the group with precipitated osseus development, one child showed on both fifth fingers the deformity of the middle phalanx that occurs in the majority of cases of Mongolism. In four of the children of the entire series there were irregularities

in the order of appearance of the ossification centers. In four cases of the first and in two of the second group the osseous development was asymmetrical in the two wrists.

The coincidence of skeletal anomalies with retarded growth in height needs further elucidation. If the growth potential of a child is established in the anlage like other constitutional characters, it is obvious that a coincidence of deviations from normal growth and skeletal anomalies may be encountered in the same person. Both may be the result of an abnormal gene with pleiotropic effects or of a combination of several such genes. The relative growth rate was below the norm in the three of our cases in which data over a longer period of observation were available. In Case 1 the increase in height from 4 7/12 to 7 1/12 years amounted only to 4¾ in. (12 cm.), the normal increase being 6 to 6½ in. (15 to 17 cm.); in Case 2 the increase from 3 4/12 to 10 years was 4¼ in. (11 cm.), normal increase being 6½ in., and in Case 5 the increase from 7 8/12 to 8 8/12 years was 1¼ in. (3 cm.), normal 2½ in. (6 cm.).

The presence of certain somatic (mostly mesenchymatous) stigmas and of deviations from the normal general growth pattern is indicative that in a questionable case of retarded growth and development the problem is not an endocrine one but is deeper seated. The simultaneous occurrence of mesenchymatous stigmas and deviations from normal growth or, in the language of genetics, the linkage in graded human characters, should be studied more carefully. There are certain somatic stigmas which are frequently encountered in children with or without gross disease or deviations from normal development. Such stigmas are fusion of ribs, particularly of the posterior medial aspects, shovel-shaped ends of the sternal extremity of the ribs, clubbing of the thumb with shortening of the distal phalanx, micrognathia, hyperextensibility of the joints, nodules on the medial aspects of the auricles, Madelung's deformity, polydactylism, fusion of vertebral bodies, cervical ribs, brachycephalia, Dupuytren's contracture, arched palate, and others. Most of these stigmas in themselves are relatively insignificant. Only in case of their accumulation in the same carrier do they deserve more attention. Many of these anomalies tend to occur in their carriers always in the same linkage and are known under special names. Although they appear to be morphologically, topographically, and embryologically quite heterogenous, by their more than fortuitous coincidence obviously they point to some common condition of origin.

More difficult is the interpretation of the plus variations of osseous development (Cases 6 through 12). The occurrence of craniotabes in five cases is more than a simple coincidence. Although craniotabes has been considered to be the first sign of rickets and often is present before other more pronounced signs, chemical changes, or characteristic roentgenogram signs manifest themselves, it is questionable whether or not craniotabes is always a sign of rickets. None of our patients revealed a single characteristic symptom of this disease. The precipitated osseous development in itself and the perfect state of calcification on roentgen examination are against rickets. The literature on craniotabes as the only manifestation of rickets is controversial. Some of the investigators of this problem are of the opinion that craniotabes always means rickets, while others consider other etiologic factors as possible and speak of "physiological craniotabes." Only Höjer [3] mentions

3. Höjer, J. A.: Acta pædiat. **5**:16, 1925.

the coincidence of craniotabes with precipitated osseous development. In one of his cases he speaks of a "sensationally precocious development" and considers the so-called physiological (better nonrachitic) craniotabes as a constitutional problem. The patient in Case 8 of this series is most contributory to the constitutional interpretation of the precocious skeletal differentiation, by showing a deformity of the middle phalanx of both fifth fingers as another skeletal anomaly. The conclusion from the cases observed is that the carriers of nonrachitic craniotabes are constitutionally abnormal children, born with a tendency toward premature skeletal differentiation. Craniotabes is only a secondary sign of this systemic deviation from normal development. As in rickets, it is the bones with the most intense growth, such as the flat bones of the calvaria, which are involved.

In Case 12 precipitated skeletal differentiation was associated with an abnormal blood picture. The relative and absolute number of polymorphonuclear white blood cells was reduced, but not the total white-blood-cell count. These findings are not characteristic of the agranulocytosis which occasionally follows the intake of sulfonamides or benzene-ring compounds.

Case 13 is interesting because of the coincidence of precipitated osseous development with a gross abnormality of the skeleton, a spina bifida occulta. In addition to the precipitated osseous development, there was also asymmetry in development, in that the distal epiphysis of the ulna was present on only one side.

This "skeleton-maturing factor" must be different from other known hormones which stimulate development, such as the pituitary, sex, or thyroid hormones. None of the children of the plus-variation group was taller than expected, nor did they reveal any signs of sex precocity. The eruption of the deciduous teeth was ahead in some of the cases. This observation should be emphasized. Eruption of teeth and skeletal maturation belong together and seem to be under the control of one and the same factor, which has no relation to the rest of the child's development. Deviations from the normal schedule of dentition with regard to time are well-known, on the plus as well as the minus side. Frequently dentition is normal in children with retarded development and not infrequently is abnormal in children who develop according to schedule in other ways.

Growth, skeletal maturation, epiphyseal ossification, and dental development are usually attributed to the activity of the thyroid gland. However, the present study favors the assumption that constitutional and genetic factors are also important.

Other phenomena which should be emphasized are disharmonic and asymmetric development. In some of the observations the order in which the ossification centers appeared deviated from the regular order in which they are supposed to appear (disharmonic), and in some the development was different on the two sides (asymmetric). This is well-known from one of the best-studied entities with multiple congenital skeletal abnormalities, Mongolism.

There is evidence that the factor which governs the differentiation of the skeleton exerts a systemic effect. The demonstrated deviation from the norm of the osseous development cannot be explained as the result of local stimulation, since it occurs bilaterally, although not always symmetrically.

SUMMARY

Retarded growth and skeletal differentiation were observed in six boys. In four of them other skeletal anomalies were detectable, in three instances pseudoepiphyses on the proximal end of both second metacarpals and in one case a radio-ulnar synostosis. In no case were any signs of an endocrine disorder present.

In seven cases advanced osseous development was described, without any other signs of precipitated development, particularly not with sex precocity or other evidence of an endocrine disorder. Their height was normal for their age. Five of these children, four of whom were girls, revealed nonrachitic craniotabes. In three cases of this group other anomalies were detectable, in one case a deformity of the middle phalanx of both fifth fingers, in another case an abnormality of the peripheral blood, and in the third case a spina bifida occulta. Early dentition was noticed in some of the patients with advanced osseous development. Pseudoepiphyses were seen only in the group with retarded development.

Disharmonic and asymmetric osseous development seems to be a frequent finding in carriers of skeletal anomalies.

The conclusion is reached that neither retarded nor advanced osseous development is always the result of an endocrine disturbance, but frequently is established in the "anlage" of the person involved. The evidence of other skeletal anomalies in the carriers of deviations from the normal pattern of osseous development is in favor of such an interpretation.

# PHYSICAL CHANGES ASSOCIATED WITH ADOLESCENCE IN BOYS

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IN A PREVIOUS paper[1] a description was given of certain physical changes accompanying adolescence in girls. The value of such information to the pediatrician was discussed, with particular reference to the normal range of individual variation in sexual maturation. In the present study a similar report is made for boys.

The general literature on adolescent bodily changes and various studies of female adolescence were cited in the earlier publication. In addition, a number of studies have dealt specifically with male adolescent development.[2] These range from concise descriptions of developmental processes to broad discussions of the relation of sexual maturation to behavior in adolescence.

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From the Fels Research Institute for the Study of Human Development, Antioch College.

1. Reynolds, E. L., and Wines, J. V.: Individual Differences in Physical Changes Associated with Adolescence in Girls, Am. J. Dis. Child. **75**:329-350 (March) 1948.

2. (*a*) Kubitschek, P. E.: Sexual Development of Boys with Special Reference to Appearance of Secondary Sexual Characters and Their Relationship to Structural and Personality Types, J. Nerv. & Ment. Dis. **76**:425-451, 1932. (*b*) Schmidt-Voigt, J.: Der gegenwärtige Eintritt und die Acceleration der Pubertätsentwicklung bie der männlichen Jugend einer Grossstadt, Ztschr. Kinderh. **61**:548-590, 1940. (*c*) Greulich, W. W.; Dorfman, R. I., and others: Somatic and Endocrine Studies of Puberal and Adolescent Boys, Monograph, Soc. Res. Child Develop., 1942, Vol. 7, No. 3. (*d*) Schonfeld, W. A., and Beebe, G. W.: Normal Growth and Variation in the Male Genitalia from Birth to Maturity, J. Urol. **48**:759-777, 1942. (*e*) Ramsey, G. V.: The Sexual Development of Boys, Am. J. Psychol. **56**:217-233, 1943. (*f*) Schonfeld, W. A.: Management of Male Pubescence, J. A. M. A. **121**:177-182 (Jan. 16) 1943; (*g*) Primary and Secondary Sexual Characteristics, Am. J. Dis. Child. **65**:535-549 (April) 1943. (*h*) Crampton, C. W.: Physiological Age: A Fundamental Principle, Child Develop. **15**:1-52, 1944. (*i*) Ellis, R. W. B.: Height and Weight in Relation to Onset of Puberty in Boys, Arch. Dis. Childhood **21**:181-189, 1946. (*j*) Seckel, H. P. G.: Precocious Sexual Development in Children, M. Clin. North America **30**:183-209, 1946; (*k*) Stuart, H. C.: Medical Progress: Normal Growth and Development During Adolescence, New England J. Med. **234**:666-672, 693-700, 732-738, 1946. (*l*) Stuart, H. C.: Physical Growth During Adolescence, Am. J. Dis. Child. **74**:495-502 (Oct.) 1947. (*m*) Ellis, R. W. B.: Puberty Growth of Boys, Arch. Dis. Childhood **23**:17-26, 1948. (*n*) Kinsey, A. C.; Pomeroy, W. B., and Martin, C. E.: Sexual Behavior in the Human Male, Philadelphia, W. B. Saunders Company, 1948. (*o*) Krogman, W. M.: The Concept of Maturity from a Morphological Viewpoint, Child Develop. **21**:25-32, 1950. (*p*) Ramsey, G. V.: Sexual Growth of Negro and White Boys, Human Biol. **22**:146-149, 1950. (*q*) Wilkins, L.: The Diagnosis and Treatment of Endocrine Disorders in Childhood and Adolescence, Springfield, Ill., Charles C Thomas, Publisher, 1950. (*r*) Hamilton, J. B.: Quantitative Measurement of a Secondary Sex Character, Axillary Hair, Ann. New York Acad. Sc. **53**:585-599, 1951.

## MATERIALS AND METHODS

The 59 boys reported on in this paper are, like the girls in the earlier study,[1] regular participants in the long-term study of growth and development under way at the Fels Research Institute for the Study of Human Development.[3] The progress of Fels Research Institute children is being followed from birth through maturity, and the records of all boys between 9 and 21 yr. of age (706 observations) are used in this report. Each boy visits the physical growth department of the Fels Research Institute on his birthday and half-birthday, and the program includes medical examination and health history, nude photographs, body measurements, roentgenograms of various joints and parts, and a recording of the development of a number of sexual characteristics.

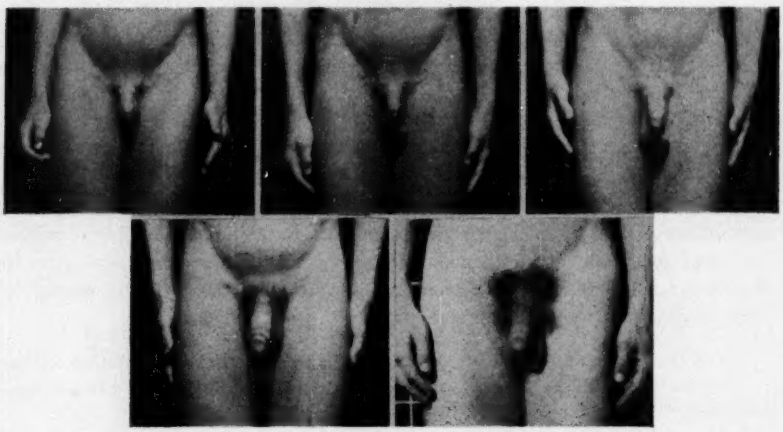

Fig. 1.—Standards for stages of genitalia maturation: (1) infantile; (2) enlargement of scrotum; (3) enlargement of penis, first "sculpturing"; (4) pronounced sculpturing and darkening; (5) adult. These standards refer to external genitalia only; pubic-hair maturation is shown in Figure 4.

The distribution of these boys, by number of consecutive semiannual examinations, is shown in the following tabulation:

| No. of examinations | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| No. of boys..... | 4 | 3 | 3 | 3 | 1 | 5 | 1 | 2 | 5 | 2 | 5 | 3 | 3 | 5 | 2 | 2 | 8 | 2 | 59 |
| Total..... | 12 | 12 | 15 | 18 | 7 | 40 | 9 | 20 | 55 | 24 | 65 | 42 | 45 | 80 | 34 | 36 | 152 | 40 | 706 |

Pictorial cues, obtained from an analysis of our series, were used to describe various stages of maturation of external genitalia, penis size and shape, and growth of pubic hair. In the older boys the regional distribution of body hair was recorded.[4]

Ratings of genitalia maturation were made on a five-point scale (Fig. 1): (1) infantile; (2) enlargement of scrotum, first reddening and texture change; (3) first "sculpturing" and enlargement of penis; (4) pronounced sculpturing and darkening; (5) essentially adult; reddish brown color, loose penile skin, loss of sharp sculpturing.

3. Sontag, L. W.: The Fels Research Institute for the Study of Human Development, Antioch College, Yellow Springs, Ohio, 1946; Biological and Medical Studies at the Samuel S. Fels Research Institute, Child Develop. **17**:81-84, 1946.

4. Reynolds, E. L.: The Appearance of Adult Patterns of Body Hair in Man, Ann. New York Acad. Sc. **53**:576-584, 1951.

Size of penis was rated on a seven-point scale. The standards are shown in Figure 2 and were applied in each case without reference to other aspects of sexual maturation. That is to say, ratings of penis size were made apart from ratings of genitalia maturation, although there is, of course, a relation between the two phenomena. For instance, no boy in our normal series

Fig. 2.—Standards for rating size of penis on a seven-point scale.

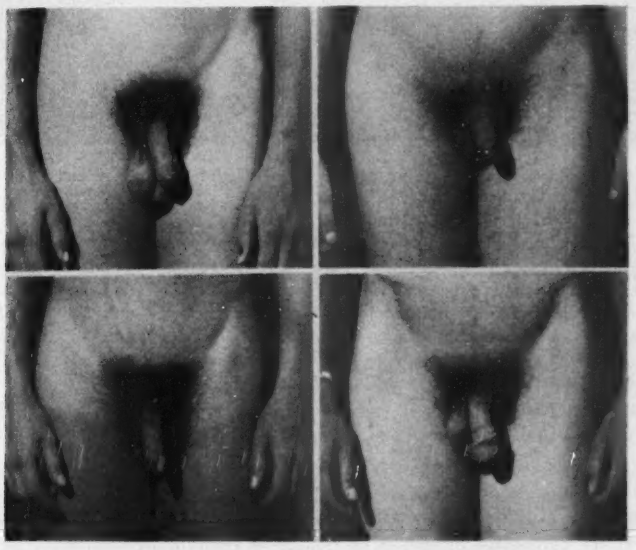

Fig. 3.—Standards for shape of penis: upper left, no unusual findings; upper right, markedly short; lower left, long, thin; lower right, glans noticeably larger than corpus.

whose genitalia were in Stage 1 (infantile) had a penis size larger than Size 4, while no boy whose genitalia were in Stage 5 (adult) had a penis size smaller than Size 4. The relation of pictorial standards to direct measurements of penis size will be discussed in a later section.

A tentative classification of shape of penis (Fig. 3) is given as the following: (1) "normal"; no unusual findings; (2) markedly short; (3) long, thin; (4) glans noticeably larger than corpus. In a few cases it was impossible adequately to classify penis shape. In spite of the difficulties in the assessment of this characteristic, it was felt that a description of even limited usefulness should be attempted, since there is some evidence that the possession of a penis of aberrant size or shape has certain psychologic implications.[5]

Growth of pubic hair, as in the girls, was rated on a five-point scale (Fig. 4): (1) infantile; (2) first appearance, pigmented, usually straight, sparse, at base of penis; (3) slight curl, slight spread, usually darker; (4) curled, moderate amount and spread, not yet extended to thighs; (5) "adult" in type, profuse, forming an inverse triangle extending to thighs corresponding to the horizontal type described by Dupertuis and co-workers.[6]

Some comments concerning the ratings should be made. First, all the standards were derived from photographs taken under similar conditions of distance, positioning, and lighting. Second, observations were obtained from longitudinal data, an average of 12 sets of semiannual photographs (front, side, and back view) being available on each boy, with a range of three to 20 sets. This permitted a check on whether a characteristic shown represented a growth or maturational change or was a transient factor induced by an immediate environmental stimulus such as temperature. It also permitted both earlier and more accurate detection of slight changes in individual boys.

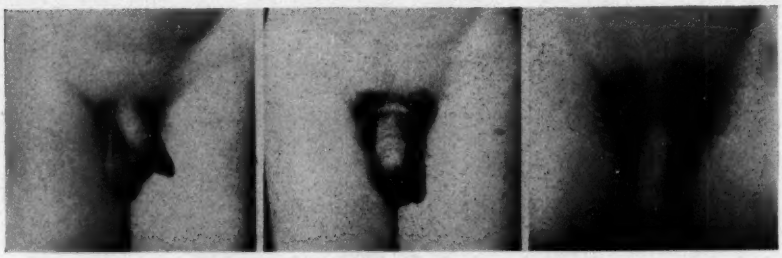

Fig. 4.—Standards for stages in maturation of pubic hair: Stages 3, 4, and 5. The infantile stage (1) and the beginning stage (2) are not shown.

Third, an attempt was made to rate each characteristic independently of other characteristics; for instance, ratings of pubic hair were made without reference to stage of maturation of genitalia. This made possible the examination of discrete elements of sexual maturation. Finally, there are differences in the reliability with which these ratings can be applied to an individual boy if he were to be seen only at a single visit. Generally speaking, ratings of genitalia maturation are somewhat more difficult to make than ratings of penis size and shape, while the stage of pubic-hair development may be determined with little difficulty.

In addition to the boys' series, photographs and observations were also taken on 50 fathers. Certain comparisons of fathers with sons will be given in a later section.

## RESULTS

*Genitalia: Maturation, Duration; Penis Size and Shape.*—Table 1 shows, by age level, the percentage of boys in each stage of genitalia maturation. The number

5. Frank, L. K.: General Considerations: Certain Problems of Puberty and Adolescence, J. Pediat. **19**:294-301, 1941. Schonfeld, W. A.: Deficient Development of Masculinity, Am. J. Dis. Child. **79**:17-29 (Jan.) 1950.

6. Dupertuis, C. W.; Atkinson, W. B., and Elftman, H.: Sex Differences in Pubic Hair Distribution, Human Biol. **17**:137-142, 1945.

TABLE 1.—*Percentage of Boys at Each Stage of Genitalia Maturation, by Age Level*

| Stage | Age, Yr. | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 9 | 9.5 | 10 | 10.5 | 11 | 11.5 | 12 | 12.5 | 13 | 13.5 | 14 | 14.5 | 15 | 15.5 | 16 | 16.5 | 17 | 17.5 | 18 | 19-21 |
| 1 ..... | 100 | 97 | 95 | 83 | 65 | 36 | 22 | 9 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2 ..... | 0 | 3 | 5 | 17 | 33 | 55 | 63 | 42 | 18 | 13 | 8 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 3 ..... | 0 | 0 | 0 | 0 | 2 | 4 | 9 | 42 | 41 | 23 | 5 | 3 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 4 ..... | 0 | 0 | 0 | 0 | 0 | 4 | 5 | 7 | 38 | 64 | 87 | 94 | 97 | 97 | 96 | 88 | 77 | 56 | 25 | 0 |
| 5 ..... | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 4 | 12 | 23 | 44 | 75 | 100 |
| No. of cases | 50 | 59 | 57 | 52 | 49 | 47 | 43 | 43 | 39 | 39 | 37 | 35 | 34 | 31 | 27 | 26 | 22 | 16 | 14 | 5 |

Total no. of cases: 736

of cases at each age level are also given. Figure 5 gives the distribution in graphic form. The average age at which each stage is attained is shown in the following tabulation:

| Genitalia Maturation, Stage | Mean Age, Yr. | Standard Deviation | Median Age, Yr. |
|---|---|---|---|
| 2 ..... | 11.5 | 0.9 | 11.3 |
| 3 ..... | 12.7 | 0.8 | 12.5 |
| 4 ..... | 13.4 | 0.7 | 13.2 |
| 5 ..... | 17.3 | 0.8 | 17.6 |

Associations between the various stages, as shown by the coefficient of correlation, range from 0.34 (between Stages 4 and 5) to 0.86 (between Stages 3 and 4).

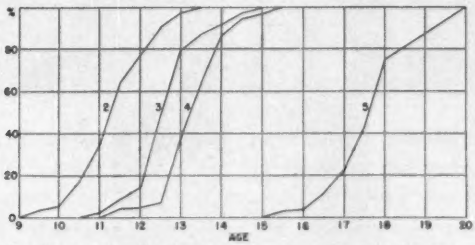


Fig. 5.—Percentage distribution for stages of genitalia maturation.

The average duration of the various stages and the range of individual cases in the present series are shown in the following tabulation:

| Period Covered | Mean, Yr. | Range for Individual Boys |
|---|---|---|
| From Stage 2 to Stage 3..... | 1.3 | From 6 mo. to 3 yr. |
| From Stage 3 to Stage 4..... | 0.6 | From 3 mo. to 1.75 yr. |
| From Stage 4 to Stage 5..... | 3.9 | From 2.5 yr. to 5 yr. |
| From Stage 2 to Stage 5..... | 5.8 | From 5 yr. to 7.25 yr. |

The average Fels Research Institute boy, therefore, took slightly less than six years to pass from beginning genitalia maturation to the adult stage. The boy who made the transition fastest in our series did it in five years, while the boy who made it slowest took over seven years to make a similar shift.

It will be noted that the transition from Stage 3 to Stage 4 is relatively rapid, while a much longer period generally elapses between the attainment of Stage 4 and the achievement of the adult stage of genitalia maturation.

Table 2 shows, by age level, the percentage of boys in each stage of penis size. The number of cases at each age level are also shown.

TABLE 2.—*Percentage of Boys in Each Category of Penis Size, by Age Level*

| | Age, Yr. | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Size | 10 | 10.5 | 11 | 11.5 | 12 | 12.5 | 13 | 13.5 | 14 | 14.5 | 15 | 15.5 | 16 | 16.5 | 17 | 17.5 | 18 | 19-21 |
| 1 | 28 | 26 | 24 | 25 | 16 | 12 | 8 | 3 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2 | 53 | 54 | 54 | 48 | 56 | 36 | 10 | 13 | 8 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 3 | 14 | 15 | 16 | 17 | 16 | 40 | 36 | 8 | 5 | 3 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 4 | 5 | 5 | 6 | 8 | 7 | 5 | 26 | 36 | 11 | 18 | 16 | 20 | 16 | 15 | 14 | 18 | 27 | 20 |
| 5 | 0 | 0 | 0 | 2 | 0 | 2 | 15 | 20 | 35 | 27 | 23 | 20 | 20 | 23 | 36 | 35 | 40 | 60 |
| 6 | 0 | 0 | 0 | 0 | 5 | 2 | 3 | 15 | 22 | 33 | 42 | 40 | 48 | 42 | 41 | 41 | 27 | 20 |
| 7 | 0 | 0 | 0 | 0 | 0 | 2 | 3 | 5 | 16 | 15 | 16 | 20 | 16 | 19 | 9 | 6 | 7 | 0 |
| No. of cases | 58 | 54 | 50 | 48 | 43 | 42 | 39 | 39 | 37 | 33 | 31 | 30 | 25 | 26 | 22 | 17 | 15 | 5 |

Total no. of cases: 614

There seems to be a tendency, in some boys, for penis size to be smaller in the adult stage of genitalia maturation than it was at its maximum size during Stage 4. The tabulation below illustrates this:

| Genitalia Maturation, Stage | Mean Size of Penis |
|---|---|
| 2 | 2.1 |
| 3 | 3.0 |
| 4 | 4.6 |
| Maximum size reached during Stage 4 | 5.9 |
| 5 | 4.9 |

Thus, the average size of penis is Size 5 at the time the adult stage of genitalia maturation is reached, but the maximum size of penis reached during the period between Stages 4 and 5 of genitalia maturation is on the average almost Size 6.

All boys do not show this size reduction, but in general the larger the penis size in Stage 4 of genitalia maturation, the likelier there is to be a decrease in penis size when the adult stage of genitalia maturation is reached. Moreover, no boy who reached penis Size 7 remained in this category by the time he had reached the adult stage of genitalia maturation.

Size changes ranged from as little as two units (Size 2 at beginning of genitalia maturation, Size 4 at maximum size, and Size 4 at adult stage of genitalia maturation) to as much as 5 units (Size 1 at beginning of genitalia maturation, Size 6 at maximum size, and Size 5 at adult stage of genitalia maturation).

The greatest size reduction noted was three size units. This boy is shown in Figure 6. At the beginning of genitalia maturation he had a penis size of 3. At 15 yr., in Stage 4 of genitalia maturation, he had a penis size of 7; at 18 yr., with genitalia at Stage 5 (adult), his penis size was reduced to Size 4. The evidence for these changes is available from the examination of serial photographs taken semiannually from 9 through 18 yr. and from an additional photograph taken at the age of 21 yr.

Another source of information has been the direct comparison of a small series of fathers with their sons. In Table 3, the mean penis size for six fathers is 4.8 and the mean adult size for their nine sons is 4.9. However, the mean maximum penis size reached by these boys during adolescence is 5.9. Also shown in Table 3 is the mean size of penis for 50 men, fathers of boys in the Fels Research Institute series, compared with the maximum and the adult size reached by the boys.

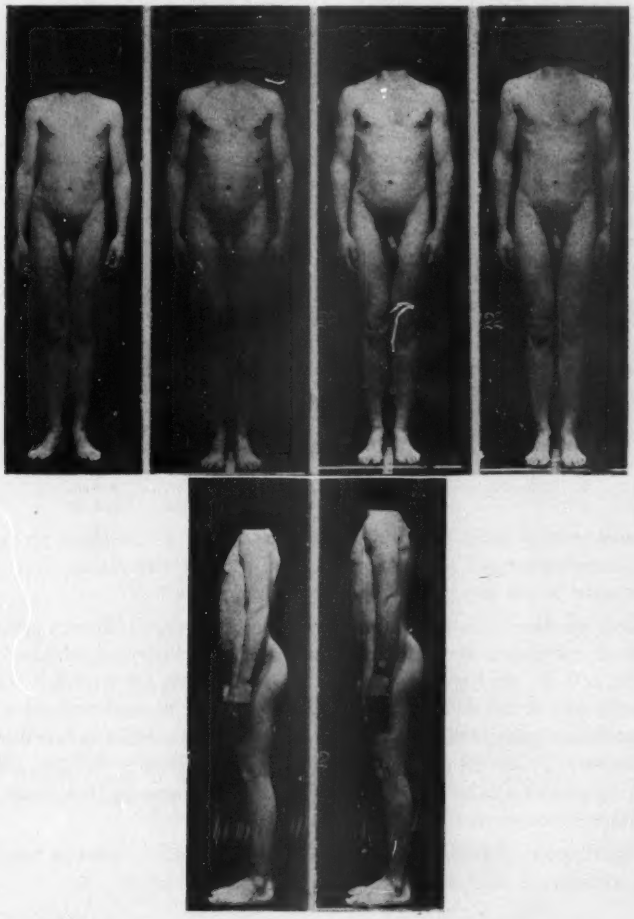

Fig. 6.—Reduction in size of penis at the adult stage of genitalia maturation. Front views of the same boy at 15, 16, 17, and 18 years of age and side views at 15 and 18 years of age.

Our continued observation on the development of Fels Research Institute boys leads us to believe that this tendency toward a reduction in penis size in later adolescence, when it occurs, is a significant developmental pattern.

TABLE 3.—*Comparison of Penis Size*

A. Comparison of Penis Size of Fathers with That of Their Sons

| Family | Father's Size | Son's Maximum Size | Son's Adult Size |
|---|---|---|---|
| A | 4 | 7 | .. |
| | | 5 | 4 |
| B | 3 | 4 | 4 |
| C | 5 | 7 | 5 |
| D | 6 | 6 | 5 |
| | | 7 | 6 |
| | | 6 | 5 |
| E | 6 | 6 | 5 |
| F | 5 | 5 | 5 |
| Mean size | 4.8 | 5.9 | 4.9 |

B. Group Comparison of Fathers and Sons

| | Maximum Size | | | Adult Size | | |
|---|---|---|---|---|---|---|
| | Mean | Standard Deviation | No. | Mean | Standard Deviation | No. |
| All fathers | ... | ..... | .. | 4.4 | ±1.0 | 50 |
| All sons | 5.9 | ±1.0 | 36 | 4.8 | ±0.6 | 12 |

In Figure 7 penis size in 24 boys, as rated from photographs, is compared with actual measurements of length of flaccid penis in these same boys. There is a general agreement between the two methods, within the ranges indicated in the following tabulation:

| Size Rating | Length of Flaccid Penis |
|---|---|
| 5 | 7- 9 cm. |
| 6 | 9-10 cm. |
| 7 | 10-12 cm. |

Circumference of penis is also a factor in assigning a size rating; a penis of smaller circumference will tend to be placed in a lower size rating, even though it has the same length as a penis of larger circumference.

We have also taken a few measurements of both stretched and erect penis. The coefficient of correlation between length of flaccid and length of stretched penis, in 24 cases, is 0.70. In Figure 8 we have plotted our data for stretched and erect penis length against the data of Schonfeld [2d] for length of stretched penis. Our measurements are consistently in the upper ranges of Schonfeld's distribution, particularly between 14 and 19 yr. We are increasing our series in this area and hope eventually to present a fuller comparison of penis size as seen in photographs, with direct measurements of flaccid, stretched, and erect penis.

The distribution of penis shape in the present series, as rated at Stage 4 of genitalia maturation, is shown in the following tabulation:

| | No. of Boys |
|---|---|
| "Normal" | 20 |
| Markedly short | 5 |
| Long, thin | 3 |
| Glans noticeably larger than corpus | 4 |
| Unclassified | 2 |

In the 50 fathers studied, 75% fell into the normal category and 25% into the short group.

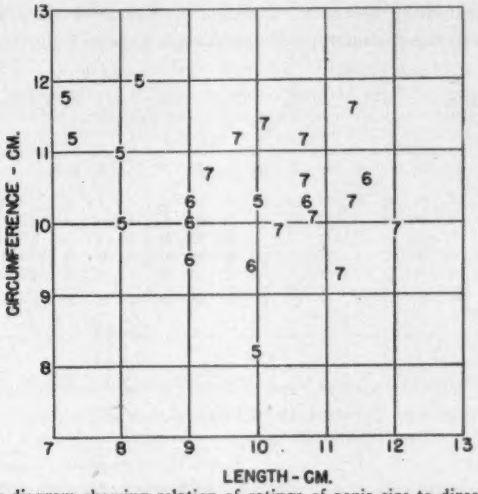


Fig. 7.—Scatter diagram showing relation of ratings of penis size to direct measurements of flaccid penis; there is a general agreement between the two methods.

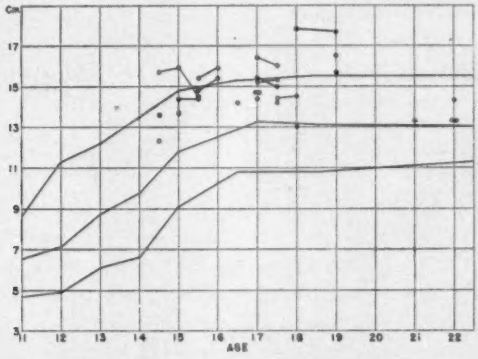


Fig. 8.—Direct measurements of stretched penis length (open circles) and length of erect penis (solid circles) for Fels Research Institute boys, as plotted against Schonfeld's values for length of stretched penis at the 10th, 50th, and 90th percentiles; connected dots represent measurements on the same boy at different ages.

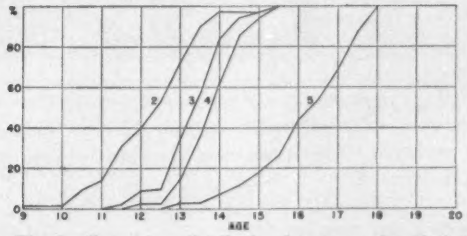


Fig. 9.—Percentage distribution for stages of pubic hair.

*Pubic Hair: Growth; Duration; Relation to Genitalia Maturation.*—Table 4 shows, by age level, the percentage of boys in each stage of pubic-hair development

TABLE 4.—*Percentage of Boys at Each Stage of Pubic-Hair Maturation, by Age Level*

| | Age, Yr. | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Stage | 8.5 | 9 | 9.5 | 10 | 10.5 | 11 | 11.5 | 12 | 12.5 | 13 | 13.5 | 14 | 14.5 | 15 | 15.5 | 16 | 16.5 | 17 | 17.5 | 18 | 19-21 |
| 1 | 100 | 98 | 98 | 98 | 91 | 86 | 69 | 60 | 48 | 28 | 10 | 3 | 3 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2 | 0 | 2 | 2 | 2 | 9 | 14 | 29 | 31 | 43 | 38 | 33 | 14 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 3 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 7 | 7 | 20 | 20 | 22 | 9 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 4 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 2 | 12 | 33 | 59 | 74 | 76 | 73 | 56 | 46 | 32 | 12 | 0 | 0 |
| 5 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 3 | 3 | 12 | 18 | 27 | 44 | 54 | 68 | 88 | 100 | 100 |
| No. of cases | 59 | 59 | 59 | 59 | 54 | 50 | 48 | 45 | 42 | 40 | 39 | 37 | 34 | 33 | 30 | 25 | 26 | 22 | 16 | 15 | 5 |

Total no. of cases: 797

and the number of boys at each age level. Figure 9 gives this distribution graphically. Norms for each stage are shown in the following tabulation:

| Pattern of Pubic Hair, Stage | Mean Age, Yr. | Standard Deviation | Median Age, Yr. |
|---|---|---|---|
| 2 | 12.2 | 1.1 | 12.4 |
| 3 | 13.3 | 0.8 | 13.4 |
| 4 | 13.9 | 0.7 | 13.8 |
| 5 | 16.1 | 1.2 | 16.3 |

Associations between the various stages, as shown by the coefficient of correlation, range from 0.50 (between Stages 2 and 5) to 0.94 (between Stages 3 and 4).

The average duration of the various stages and the range of individual cases in the present series are shown in the following tabulation:

| Period Covered | Mean, Yr. | Range for Individual Boys |
|---|---|---|
| From Stage 2 to Stage 3 | 1.1 | From 3 mo. to 3.25 yr. |
| From Stage 3 to Stage 4 | 0.6 | From 3 mo. to 1.25 yr. |
| From Stage 4 to Stage 5 | 2.2 | From 1 yr. to 4 yr. |
| From Stage 2 to Stage 5 | 3.9 | From 2 yr. to 6 yr. |

The average Fels Research Institute boy thus took about four years to reach the adult pattern of pubic-hair distribution, after the first appearance of pubic hair. The fastest transition in our series was in two years, the slowest in six years.

Considering both genitalia maturation and the development of pubic hair, the following is the commonest sequence of appearance of the various stages:

| Item | Approximate Age, Yr. |
|---|---|
| 1. Genitalia 2 (enlargement of scrotum, etc.) | 11.5 |
| 2. Pubic Hair 2 (first appearance) | 12.0 |
| 3. Genitalia 3 (enlargement of penis, etc.) | 12.5 |
| 4. Pubic Hair 3 (slight curl and spread) and Genitalia 4 (sculpturing and darkening) | 13.5 |
| 5. Pubic Hair 4 (curled, moderate amount and spread) | 14.0 |
| 6. Pubic Hair 5 (adult) | 16.0 |
| 7. Genitalia 5 (adult) | 17.5 |

The above sequence is followed exactly by only 12 boys, indicating the great range of individual variation. The commonest reversals between adjacent stages are:

| | |
|---|---|
| Genitalia 3 before Pubic Hair 2 | 41% |
| Genitalia 4 before Pubic Hair 3 | 32% |

Genitalia maturation began before the appearance of pubic hair in 70% of the cases examined; in 16% the two processes began at approximately the same age, and in 14% pubic hair appeared before genitalia maturation could be observed.

Genitalia maturation, therefore, tends to begin earlier (around 11.5 yr.) and to reach the adult stage later (around 17.5 yr.) than does the development of pubic

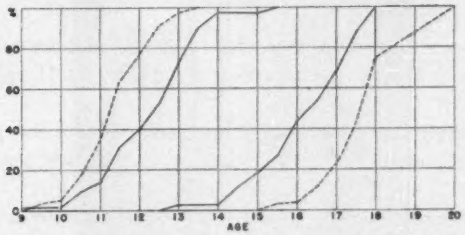


Fig. 10.—Percentage distribution for Stage 2 (beginning) and Stage 5 (adult) for genitalia maturation (broken lines) and development of pubic hair (solid lines).

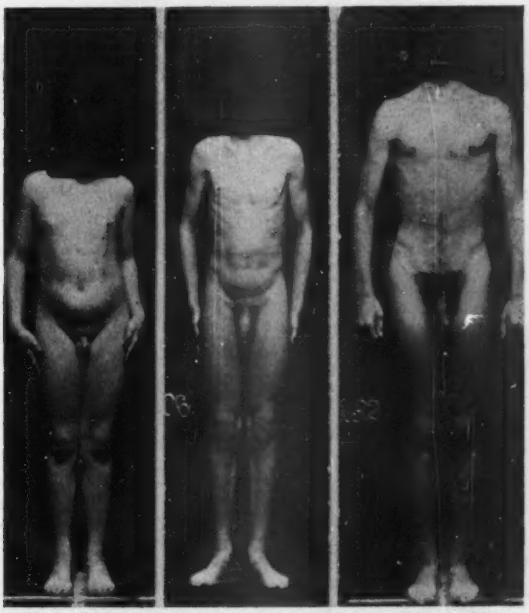

Fig. 11.—Individual differences in sexual maturation: a late-maturing boy (left photograph), a boy in the middle range (center photograph), and an early-maturing boy (right photograph); all three boys are 14 years old.

hair (beginning around 12 yr., adult around 16 yr.). This is shown graphically in Figure 10, in which the beginning and the adult stages for both characteristics are plotted on the same graph.

*Individual Differences in Maturation.*—The range of individual differences in timing of maturational processes in our normal series is illustrated in Figure 11, with a comparison of a late-maturing boy, a boy in the middle range, and an early-maturing boy. In each case the photograph is of the boy at the age of 14 years.

At this age, the early-maturing boy is in Stage 4 of genitalia maturation and Stage 5 of pubic hair. Penis is Size 7. Genitalia maturation began prior to 11 yr., and pubic hair appeared at 11 yr.

The boy in the middle range shows, at 14 yr., Stage 4 for both genitalia and pubic hair. Penis is Size 6. Genitalia maturation began at 11 yr., and pubic hair appeared at 12.5 yr.

The late-maturing boy is in Stage 2 for both genitalia and pubic hair, with penis in Size 2. Genitalia maturation began at 13.5 yr., and pubic hair has just appeared at 14 yr.

In Figure 12 further individual differences in maturation are shown. Both boys have penis Size 4, but one is still in Stage 1 (infantile) in genitalia maturation, while the other boy is in Stage 5 (adult). Size of penis alone, therefore, is inadequate as a criterion of maturational status, because of the wide individual differences which exist.

The boys so far discussed represent cases taken from our normal series. In contrast, Figure 13 shows photographs of two boys well beyond our normal limits, who were referred to the Fels Research Institute for special observation.

The first of these boys was referred to the Fels Research Institute as a case of adrenal hyperplasia. His chronological age was 2 yr.; his height the equal of a 3-yr.-old boy, and his weight that of a 4-yr.-old boy. His skeletal age was about 7 yr. The premature enlargement of the penis and the beginning growth of coarse, straight blond hairs at the base of penis may be seen, as well as the lack of growth of testicles.

The other boy was 17 yr. at the time of his visit and was referred to us as a case of pituitary dwarfism, combined with thyroid deficiency. His height was the equivalent of that of a 9-yr.-old boy and his weight that of a boy 10.5 yr. of age. He had a skeletal age between 11.5 and 12 yr. The undeveloped genitalia and lack of pubic hair may be seen.

*Further Comparisons of Boys Showing Various Maturational Extremes.*—In this section, small series of boys from opposite ends of maturational distributions are compared: in Figure 14, boys with profuse body hair at 18 yr. (three), with boys having slight body hair at 18 yr. (four); in Figure 15, boys whose duration of maturation between Genitalia 2 and 4 lasted at least three years (four), with boys whose comparable maturation lasted a year or less (two); in Figure 16, boys whose duration of maturation between Pubic Hair 2 and 4 lasted at least three years (three), with boys whose comparable maturation lasted a year or less (three).

Each chart shows ages at first appearance of pubic hair and beginning of genitalia maturation and at Stage 4 for these two items, as well as penis size at Stage 2 of genitalia maturation and at maximum size of penis. The values charted are the averages for each subgroup, and the vertical arrows show the mean and standard deviation for the entire series.

Fig. 12.—Individual differences in the relation of sexual maturation to penis size: both boys have penis Size 4, but the boy at the left is in Stage 1 (infantile) for both genitalia maturation and pubic hair, while the boy at the right is in Stage 5 (adult).

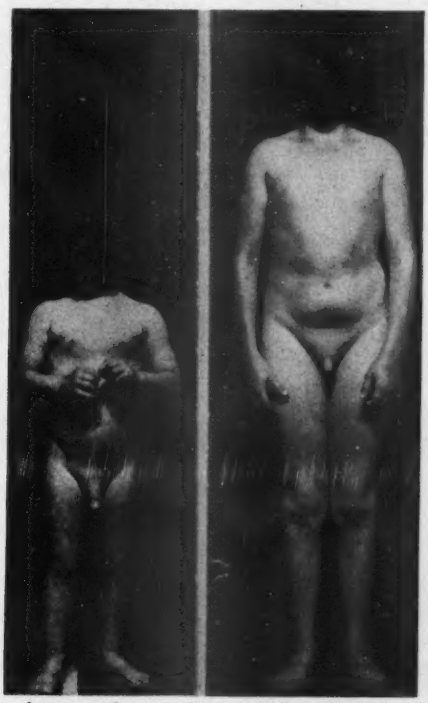

Fig. 13.—Two boys whose sexual maturation is outside our normal series, who were referred to the Fels Research Institute for special observation (details given in text).

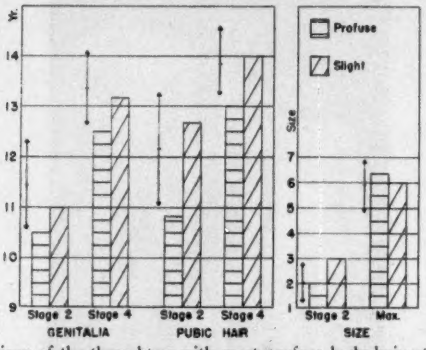


Fig. 14.—Comparison of the three boys with most profuse body hair at 18 years and the four boys with least body hair at 18 years, for mean age at Stage 2 (beginning) and at Stage 4 of genitalia maturation, mean age at Stage 2 (beginning) and at Stage 4 of pubic hair, and mean size of penis at Stage 2 of genitalia maturation and at maximum size of penis. The vertical arrows represent the range of one standard deviation on either side of the mean for the entire series.

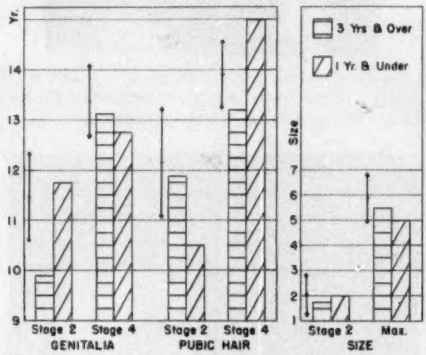


Fig. 15.—Boys whose duration of maturation (as measured by genitalia development) was long (four), compared with boys whose comparable duration of maturation was short (two); Figure 14 gives details.

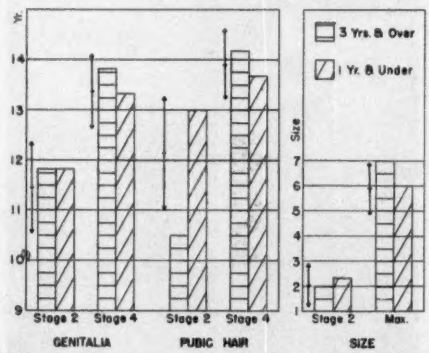


Fig. 16.—Boys whose duration of maturation (as measured by development of pubic hair) was long (three), compared with boys whose comparable duration of maturation was short (three); Figure 14 gives details.

The boys with profuse body hair at 18 yr. were somewhat earlier, both in genitalia maturation and in development of pubic hair, particularly in first appearance of pubic hair. In terms of penis size, they averaged one unit smaller at the beginning of genitalia maturation but were slightly larger at the time of maximum penis size (Fig. 14).

Boys with a long "duration of maturation," using genitalia as a criterion, show a much earlier beginning genitalia maturation but are only slightly older at Genitalia 4. Boys with a long maturation period for genitalia have a much shorter developmental period for pubic hair, while those boys who pass from Genitalia 2 to 4 in a very short period show a long developmental span for pubic hair. There is little difference between the two groups in penis size (Fig. 15).

Boys with a long "duration of maturation," using pubic hair as a criterion, show little difference in genitalia maturation from boys whose comparable development of pubic hair was rapid. The longer duration seems to be chiefly a result of an earlier appearance of pubic hair, rather than of reaching Stage 4 at a much

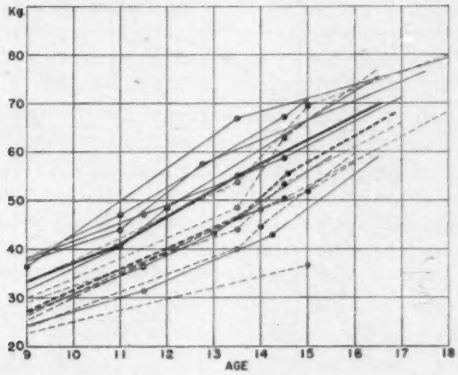


Fig. 17.—Individual growth patterns in weight for the seven earliest-maturing boys (solid lines) and the seven latest-maturing boys (broken lines) in the series. Points plotted represent weight at chronological age of 9 years, first appearance of pubic hair (open circles), Stage 4 of pubic hair (solid circles), and age at last measurement taken.

later age. There is little difference between the two groups in mean penis size at Genitalia 2, but the group with the long maturation span have a penis size at maximum averaging one unit larger (Fig. 16).

Two other comparisons of boys showing extremes of development were made, with negative results. There was no great difference, in the items compared, between boys showing extremes of penis size at Genitalia 2, or at time of maximum growth. Graphs for these two items are not shown.

*Weight, Height, and Body Build.*—In the earlier study of girls [1] reference was made to a number of studies concerned with the relation of sexual maturation to various aspects of weight, height, and body build. Figure 17 shows individual patterns of weight progress in seven early-maturing and seven late-maturing boys, based on age at first appearance of pubic hair. In the early-maturing group, mean age at first appearance of pubic hair was 10.9 yr. and genitalia maturation began

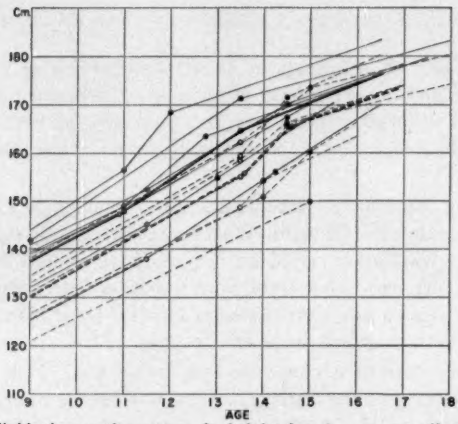


Fig. 18.—Individual growth patterns in height for the seven earliest-maturing boys (solid lines) and the seven latest-maturing boys (broken lines) in the series; Figure 17 gives details.

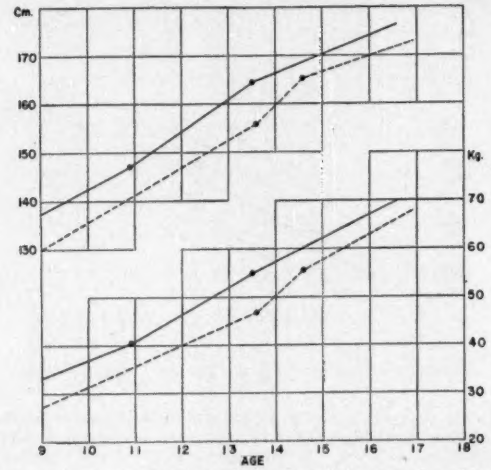


Fig. 19.—Average growth patterns for weight and height, data from Figures 17 and 18.

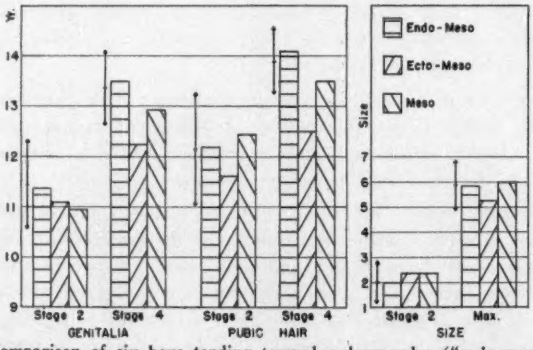


Fig. 20.—Comparison of six boys tending toward endormorphy ("endo-meso"), four boys tending toward ectomorphy ("ecto-meso"), and six boys showing marked mesomorphy ("meso"). Figure 14 gives details.

at 11.1 yr. In the late-maturing group these means were 13.6 and 12.0 yr. respectively. The early-maturing group had a mean age of 13.5 yr. and the late-maturing group a mean age of 14.6 yr. at reaching Stage 4 of pubic hair.

For both weight and height, four points were plotted: the chronological age of 9 yr., age at first appearance of pubic hair, age at Pubic Hair 4, and age at the last measurement taken. In Figure 18 individual patterns of height progress are shown for these same boys; Figure 19 gives the averages for the two groups for both weight and height, using the data of Figures 17 and 18.

Several differences between the growth patterns of early-maturing and late-maturing boys may be seen by inspection of these graphs: early-maturing boys are on the average both heavier and taller than late-maturing boys, throughout the period studied, although there is some overlapping in individual cases; late-maturing boys tend to close the gap during their period of rapid growth, but not completely so; in both groups there is an acceleration in growth between Pubic Hair 2 and 4, which is more marked during the shorter span of time covered by the late-maturing boys. In general, differences in weight and height between early-maturing and late-maturing boys are in the same direction, but are not as marked, as like comparisons in girls.

In Figure 20 boys showing different types of body build are compared. The classification used by Sheldon and others [7] was adapted to this younger group. Six boys showed marked mesomorphy (rugged build, muscularity); six boys tended toward endomorphy (soft roundness), and four boys had a noticeable degree of ectomorphy (fragile linearity). In the latter two groups, however, there is, in these adolescent boys, also a strong mesomorphic component, so they could more properly be called mesomorphic endomorphs and mesomorphic ectomorphs.

In the present series the boys tending toward endomorphy were nearest the group norms and tended to be later than the other two groups in development of genitalia and pubic hair. The boys showing ectomorphy were earlier in development and were the most aberrant. There was little difference between the three groups in size of penis at Genitalia 2, while the ectomorphic group was slightly smaller at maximum size of penis.

*Other Maturational Items.*—Information has been gathered on a number of other maturational items, on which less regular observations have been made. Our data on axillary hair are not complete, and the working out of regular stages was not attempted. In general, our observations of development of axillary hair are in line with the findings of other investigators.[8]

We have noted marked breast development during adolescence in only two boys, although a slight degree of development is rather common. In both cases there was a recession at later age levels. Since male adolescent breast development, when it appears, is often an event of fairly short duration, it is possible that our observations, made at six-month intervals, may have missed some cases.

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7. Sheldon, W. H.; Stevens, S. S., and Tucker, W. B.: The Varieties of Human Physique, New York, Harper & Brothers, 1940. Seltzer, C. C., and Gallagher, J. R.: Somatotypes of an Adolescent Group, Am. J. Phys. Anthropol. **4**:153-168, 1946. Sheldon, W. H.; Hartl, E. M., and McDermott, E.: Varieties of Delinquent Youth, New York, Harper & Brothers, 1949. Reynolds, E. L., and Asakawa, T.: A Comparison of Certain Aspects of Body Structure and Body Shape in 200 Adults, Am. J. Phys. Anthropol. **8**:343-365, 1950.

8. Greulich, Dorfman, and others.[2e] Schonfeld.[2g]

The appearance and distribution of body hair in the older boys were recorded.[4] The percentage of boys having hair in various areas of the body, at three age levels, is shown in the following tabulation:

| Area | 14 Yr. | 16 Yr. | 18 Yr. |
|---|---|---|---|
| Pubic | 97 | 100 | 100 |
| Axillary | 40 | 97 | 100 |
| Anterior leg | 46 | 90 | 100 |
| Posterior leg | 38 | 77 | 95 |
| Posterior thigh | 35 | 40 | 95 |
| Anterior thigh | 30 | 67 | 95 |
| Forearm | 14 | 37 | 80 |
| Abdomen | 14 | 37 | 75 |
| Buttocks | 14 | 33 | 50 |
| Chest | 3 | 7 | 40 |
| Lower back | 3 | 7 | 20 |
| Arms | 0 | 0 | 10 |
| Shoulders | 0 | 0 | 0 |

Circumcision appeared to have no relation to maturational factors studied, and there were no significant differences found between the 29 uncircumcised and the 38 circumcised boys studied.

In four boys there is a history of semi-erections at a number of visits. This is noted routinely on the physical examination record, and can also be seen readily in the photographs. In all, 18 boys, at one time or another, showed a noticeable degree of erection during some phase of the program. Physically speaking, these boys cannot be distinguished from the rest of the Fels Research Institute series.

Our work to date has convinced us of the need and value of more objective measurements and more systematized observations than are usually available on adolescent children. For instance, although ratings of genitalia size from photographs provide useful information, direct measurements of penis and testicle size are preferable, whenever it is feasible to obtain them. Color photographs are more informative than the usual black and white. We have also taken a number of infrared photographs on young adolescents, which have given promising results, particularly in the study of beginning breast development.

We are at present working out an examination form particularly adapted to adolescence which will, we hope, provide us with a more complete and accurate picture of the range of individual variability in growth and maturation during this important period.

## SUMMARY

This report is a companion article to a previously published study on girls.[1] Various aspects of individual variation in male sexual maturation are described and illustrated, based on an analysis of data obtained from 706 semiannual examinations of 59 boys who are regular participants in the longitudinal growth program of the Fels Research Institute for the Study of Human Development.

Included in the discussion are maturation of external genitalia, size and shape of penis, development of pubic hair, and interrelations of these maturational features. A comparison of boys representing various types of maturational extremes is given. The relation of body build and growth progress in weight and height to sexual maturation is discussed briefly.

Standards for rating genitalia maturation and development of pubic hair are illustrated, and the average ages at which the various stages are reached are given, as well as the distribution of these stages at half-year intervals. Standards are also illustrated for rating penis size on a seven-point scale and for describing penis shape.

Individual differences in sexual maturation are described, and examples of maturational asymmetries are shown. Boys showing extremes in the development of body hair, in the duration of maturation, and in three types of body build are compared. Individual and group patterns of weight and height in early-maturing and in late-maturing boys are also shown.

The observations in the present study of boys, as in the previous study of girls, are chiefly descriptive and classificatory in nature, and only a portion of the data on sexual maturation now being collected are discussed.

The materials here presented were selected so as to provide information which it is hoped will be useful to the clinician interested in the growth of adolescent boys.

# USE OF DESOXYCORTICOSTERONE ACETATE IN DEHYDRATION AND MALNUTRITION IN INFANCY

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THE CASES to be reported cannot be considered proved cases of adrenal cortical hypoplasia or deficiency. The patients did, however, have many of the symptoms of adrenal cortical deficiency, and they did respond to desoxycorticosterone acetate and salt therapy usually after other forms of treatment had failed. Unfortunately, there was a lack of sufficient laboratory data, especially of serum potassium, sodium, and chloride levels and of electrocardiograms.

At present three clinical syndromes due to disturbances in adrenal cortical secretions are recognized, according to Deamer and Silver,[1] namely, (1) hypofunction of the adrenal cortex causing disturbance of the salt-controlling and water-controlling hormone (Addison's disease), (2) hyperfunction of the adrenal cortex leading to masculinization and precocious maturation (excess androgen secretion), and (3) the combination of an excess of one hormone—androgen—and the simultaneous deficiency of the other—the salt and water hormone. Cushing's syndrome may be considered a fourth possibility. Here there is a simple adrenal hyperfunction which is manifested by edema, hypertension, and hyperglycemia usually with glycosuria.

The patients to be described varied from 3½ weeks to 12 months of age and presented only the findings of salt and water disturbance, with none of those of the androgenic hormone. It must be recognized that the latter symptoms may appear later than the former. The administration of desoxycorticosterone acetate and salt was for only short periods, so that the adrenal cortical deficiency, if present, was only temporary. Fanconi and Landolt[2] and Jaudon[3] advanced the theory that such temporary dysfunction can occur during infancy.

The symptoms and findings of adrenal cortical hypofunction may simulate those of many other seemingly unrelated conditions. The early regurgitation, vomiting, and weight loss may simulate those of pyloric stenosis. There are failure to gain

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The desoxycorticosterone acetate used in this study was percorten,® 5 mg. per cubic centimeter of sesame oil, manufactured by Ciba Pharmaceutical Products, Inc., Lafayette Park, Summit, N. J.

1. Deamer, W. C., and Silver, H. K.: Abnormalities in Secretion of Adrenal Cortex, J. Pediat. **37**:490, 1950.

2. Fanconi, G., and Landolt, R. F.: Manifestations of Dyscortism in Infants, Abstr. World Med. **6**:597, 1949.

3. Jaudon, J. D.: Addison's Disease in Children, J. Pediat. **28**:737, 1946.

and a poor growth record. There may be diarrhea, but dehydration is always present. The infants are weak and hypotonic and have anorexia.

The results of laboratory examinations may be of aid in the diagnosis of adrenal cortical hypofunction. The serum sodium and chloride values are usually low (normal for sodium is 137 to 146 mEq. per liter; normal for chlorides, 98 to 105 mEq. per liter). Serum potassium is usually higher than the normal of 4 to 5 mEq. per liter. The serum carbon dioxide combining power is depressed, and the nonprotein nitrogen is increased. The blood eosinophiles may be increased. The 17-ketosteroids in the urine are normal when no genital changes are present. These laboratory findings, however, are not diagnostic for adrenal cortical hypofunction alone.

There may be characteristic changes in the electrocardiogram if the serum potassium rises above 7.0 mEq. per liter. There are elevation of the T waves with a narrow base, broadening of the QRS complex, and depression of the ST segment. When changes are marked, there may be heart block. Kyle and Knop [4] state that there will be no electrocardiogram changes if the serum potassium is below 6.8 mEq. per liter, that there may be occasional changes when rises to 6.8 to 7.6 mEq. per liter occur. Regular changes occur after the potassium rises to 7.6 mEq. per liter, and the changes are dangerous when a level of 10.5 mEq. per liter is reached.

Determination of total blood eosinophiles reveals a drop in eosinophiles with the release of adrenal corticosteroids into the blood stream. In our laboratory eosinophile counts were done by the Forsham [5] method in three of the 10 cases to be presented.

It is common to obtain a history of similar symptoms in other siblings. There is usually no abnormal pigmentation of the skin. Hypoglycemia is usually present in proved cases of adrenal insufficiency.

Desoxycorticosterone acetate (percorten®) was used in each of the following 10 cases. Fluids given intravenously were isotonic sodium chloride, 5% dextrose in water, 1/6 M sodium lactate, and 1/6 M ammonium chloride in isotonic sodium chloride, the proper fluid being used to correct the acidosis or alkalosis. Darrow's solution was administered subcutaneously or orally after 24 hours of treatment with the aforementioned solutions.

## REPORT OF CASES

CASE 1.—E. W., a 1-year-old white boy, was admitted to the Children's Memorial Hospital July 25, 1949, with the diagnosis of a possible fibrocystic disease of the pancreas. He had had two previous admissions for severe upper respiratory tract infections and foul-smelling stools. He had been on a celiac diet, but during the previous six weeks there had been a weight loss of 2 lb. (907 gm.) with only one stool a day and no cough. The weight on admission was 14 lb. 10½ oz. (6,700 gm.).

On physical examination there were pallor, malnutrition, poor tissue turgor, protuberant abdomen, flat buttocks, and the inability to sit alone. The blood count, urinalysis, chest roentgenogram, barium-enema study, and trypsin and amylase values of duodenal drainage were all normal. The trypsin digestion of x-ray film by the stool was positive. The vitamin A curve

4. Kyle, L., and Knop, C.: Simulation of Cardiac Disease by Adrenocortical Failure in Infants, New England J. Med. **243**:681, 1950.

5. Forsham, P. H.; Thorn, G. W.; Prunty, F. T. G., and Hills, A. G.: Clinical Studies with Pituitary Adrenocorticotrophin, J. Clin. Endocrinol. **8**:15, 1948.

was flat. The fat content of the dried stool was 76%. The Mantoux reaction was negative. On July 30, the nonprotein nitrogen was 38 mg. per 100 cc. and the total proteins were 5.6 gm. per 100 cc. with an albumin-globulin ratio of 4.2:1.2. On Aug. 15, the serum sodium was 147 mEq. per liter, the potassium was 5.5 mEq. per liter, and the sugar was 73 mg. per 100 cc.

Treatment consisted in administration of fluids intravenously, plasma, blood, vitamin B, antibiotics, triple strength pancreatin (panteric® granules), polyvitamins, and a celiac diet. During a month of this therapy there was a continuous weight loss.

On Aug. 26 the weight was 12 lb. 15 oz. (5,900 gm.), at which time daily administration of desoxycorticosterone acetate, 5 mg., and sodium chloride, 1 gm., was started. This therapy was continued until Sept. 3, at which time the weight had increased to 14 lb. 10½ oz. The patient was discharged on a celiac diet and has continued to do well.

Although it must be remembered that patients with celiac disease are very hydrolabile, the gain of 1 lb. 11½ oz. (780 gm.) in nine days in a patient who had continued to lose weight over a period of several weeks on a controlled diet is impressive. Clinical improvement started with desoxycorticosterone acetate and sodium chloride therapy.

Case 2.—J. C., a Negro boy 6 weeks of age, was admitted to the Children's Memorial Hospital July 7, 1950, with a history of loose stools for the previous 24 hours. The birth weight was 5 lb. 2 oz. (2,300 gm.); the admission weight was 5 lb. 4 oz. (2,400 gm.). The infant was malnourished and severely dehydrated. Blood count, serologic study and urinalysis showed normal results. There were no pathogens on stool cultures. No blood chemistry studies were done.

Treatment consisted in administration of fluids intravenously, blood, plasma, antibiotics, and various formulas. By July 25 the weight had increased to 6 lb. (2,700 gm.), but the diarrhea was still present. Desoxycorticosterone acetate, 2.5 mg., and sodium chloride, 1 gm., were given daily for three days, at the end of which time the weight was 6 lb. 11¼ oz. (3,000 gm.). The diarrhea had subsided.

This infant gained 11¼ oz. (320 gm.) in three days while on desoxycorticosterone acetate therapy and was discharged well.

Case 3.—B. N., a 3-week-old white girl, was admitted to the Children's Memorial Hospital on Jan. 27, 1950, with a history of failure to gain. There had been no vomiting or diarrhea. The birth weight was 6 lb.; the admission weight was 5 lb. 3 oz. (2,350 gm.). The only finding was that of malnutrition. Blood count, serologic study, and urinalysis gave normal results. The tuberculin reaction was negative. The nonprotein nitrogen was 34 mg. per 100 cc. No other blood chemistry studies were done.

She was put on adequate formulas, but by Feb. 7 her weight had increased only to 5 lb. 6 oz. (2,440 gm.). She was therefore started on desoxycorticosterone acetate, 1.25 mg., and sodium chloride, 2 gm., therapy daily. This was continued for eight days. At the same time administration of vitamin B complex, fluids parenterally, and crude liver extract was started. During this period of therapy the weight increased to 6 lb. 9 oz. (2,980 gm.).

This infant gained 1 lb. 2¾ oz. (430 gm.) in seven days while on desoxycorticosterone acetate therapy, and she was eating well when discharged on March 4.

At the time of discharge the weight was 7 lb. 2 oz. (3,200 gm.), and this infant has continued to do well.

Case 4.—T. S., a 17-day-old Negro boy, was admitted to the Children's Memorial Hospital on May 10, 1950, with a history of vomiting since birth. Physical examination was negative except for malnutrition and moderate dehydration. The birth weight was 5 lb. 11 oz. (2,600 gm.); the admission weight was 4 lb. 15 oz. (2,200 gm.). The family history was negative.

The blood count, serologic study, and urinalysis showed normal results. The tuberculin reaction was negative. Fluoroscopy of the gastrointestinal tract and intravenous pyelograms gave normal results.

The infant continued to vomit several different formulas, even when gavage feeding was tried. Atropine and phenobarbital had no effect. Fluids, blood and plasma were given intravenously. On May 17, 1950, the weight was 4 lb. 13 oz. (2,170 gm.). The carbon dioxide combining power was 25 mEq. per liter. No other blood chemistry studies were done. At this time desoxycorticosterone acetate, 2.5 mg., and sodium chloride, 1 gm., were given daily for

14 days. The weight then increased to 5 lb. 10 oz. (2,500 gm.). The infant now retained all feedings and was discharged June 2, weighing 7 lb. 6 oz. (3,300 gm.).

This infant was readmitted to the hospital three weeks later with a history of diarrhea for one week. His weight was 7 lb. 6 oz. There was moderate dehydration. Fluids intravenously, blood, plasma, and streptomycin were given, but within the next five days the weight had decreased to 7 lb. 2 oz. The diarrhea and vomiting were still present. He was again given desoxycorticosterone acetate, 2.5 mg., and sodium chloride, 1 gm. daily for 11 days. During this therapy the vomiting and diarrhea ceased, and he began to eat well. He gained 15½ oz. (440 gm.) in 11 days and has continued to do well since his discharge. Stool cultures were negative for pathogens.

During his first period of therapy consisting of desoxycorticosterone acetate and sodium chloride this infant gained 12 oz. (340 gm.) in 14 days, and during the second period of this therapy he gained 15½ oz. in 11 days. In both instances there was marked improvement within 24 hours after the beginning of therapy.

Case 5.—J. D., a 7-week-old white girl, was admitted to the Children's Memorial Hospital July 17, 1950, with a history of diarrhea and a cold of 10 days' duration. The birth weight was 6 lb. 3 oz. (2,800 gm.); on admission the weight was 6 lb. 13 oz. (3,100 gm.). There were moderate malnutrition and severe dehydration. The infant was in shock. Serologic study, urinalysis, and blood and stool cultures showed normal results. A chest roentgenogram and an electrocardiogram were normal. The blood count was normal. On admission the carbon dioxide combining power was 20.9 mEq. per liter. Two days later it was 26.9 mEq. per liter. Treatment consisted in administration of fluids intravenously, blood, plasma, antibiotics, and various formulas.

Nine days after admission there was still a moderate dehydration, and no weight gain had occurred. The blood chlorides were 236 mEq. per liter, and the carbon dioxide combining power was 16.7 mEq. per liter. Administration of desoxycorticosterone acetate, 2.5 mg., and sodium chloride, 1 gm., was started daily and continued for seven days, followed by one-half this dose for the next three days. The diarrhea promptly subsided, and there was a weight gain of 17 oz. (480 gm.) in 11 days. At discharge on Aug. 17, the weight was 8 lb. 2 oz. (3,700 gm.). The infant has continued to do well.

The dehydration and diarrhea rapidly disappeared with the desoxycorticosterone acetate therapy. The carbon dioxide combining power increased from 16.7 to 25 mEq. per liter in three days. After a continuous loss of weight for nine days on other forms of therapy, there was a gain of 17 oz. in 11 days.

Case 6.—T. J., a 1-day-old white boy, was first admitted to the Children's Memorial Hospital on June 20, 1950, for repair of an imperforate anus. He made an uneventful recovery after surgery except for minimal weight loss and was discharged June 30, weighing 6 lb. 3 oz. which was 6½ oz. (184 gm.) below birth weight. He was readmitted to the hospital July 7, 1950, with severe diarrhea and vomiting of five days' duration. He was markedly dehydrated and malnourished, weighing 5 lb. 4 oz. Blood count, urinalysis, and the vitamin A curve were normal. Stool cultures were negative for pathogens.

Therapy consisted in administration of fluids intravenously, blood, plasma, vitamins, and adequate formulas. There was a rapid gain which then slowed down. By the end of three weeks he had gained 14 oz. (400 gm.).

On July 27 he weighed 6 lb. 2 oz. (2,780 gm.). At this time he was put on daily desoxycorticosterone acetate, 5 mg., and sodium chloride, 1 gm., therapy, and this therapy was continued until July 31. At this time he weighed 7 lb. 14 oz. (3,600 gm.). On July 26 the carbon dioxide combining power was 26.6 mEq. per liter. After this therapy was stopped, he began to lose weight and on Aug. 4 he weighed 6 lb. 10½ oz. (3,000 gm.). He was again given desoxycorticosterone acetate, 2.5 mg., daily, but without sodium chloride, until Aug. 11, at which time he weighed 6 lb. 14 oz. (3,100 gm.). He was discharged Aug. 16 weighing 6 lb. 15 oz. (3,150 gm.) and has continued to do well.

In this patient there was a rapid gain in weight with correction of the dehydration followed by a failure to gain. On therapy consisting in desoxycorticosterone acetate and sodium chloride administration, there was a weight gain of 1¾ lb. (790 gm.) in four days. During the following week he lost 1 lb. 3½ oz. (550 gm.), owing, undoubtedly, to loss of edematous fluid. Although this patient was again started on desoxycorticosterone acetate therapy, sodium chloride was not

added, and there was a resumption of weight gain. We think this would have started without desoxycorticosterone acetate, as sodium chloride was not added.

CASE 7.—R. B., a 7-day-old white boy, was admitted on June 29, 1950, weighing 7 lb. 14 oz., because of occasional vomiting, moderate abdominal distention, and absence of bowel movements. After admission he started to have stools and took his formula well. A sibling had died of meconium ileus. He was discharged July 3, weighing 7 lb. 10 oz. (3,500 gm.).

This patient was readmitted July 9 because of vomiting and infrequent stools. Hard feces were felt in both lower quadrants and a diagnosis of agenesis of the myenteric plexus was made. There was no response to medical management. On July 29 a transverse colostomy was performed. On July 28, the carbon dioxide combining power was 41.2 mEq. per liter, the serum calcium was 3.3 mEq., the serum phosphorus was 2.3 mEq., and the serum chlorides were 102.5 mEq. The carbon dioxide combining power was 34.5 mEq. per liter on July 31. The infant continued to do poorly.

On Aug. 8 he weighed 6 lb. 14 oz., and he received desoxycorticosterone acetate, 2.5 mg., and sodium chloride, 1 gm., daily until Aug. 19. From this time until Sept. 12 he was given the same dose three times a week, and from Sept. 12 to Sept. 18 he was given the same dose daily. He did not do well, although his weight increased to 7 lb. 10 oz. He died on Sept. 18. The findings at necropsy were those of malnutrition and agenesis of the myenteric plexus of the colon. The adrenals were not considered abnormal.

This infant showed little or no response to the desoxycorticosterone acetate and sodium chloride.

CASE 8.—R. L., a 1-day-old white boy, was first admitted to the Children's Memorial Hospital on July 24, 1950, for repair of an imperforate anus. The weight was 6 lb. 10 oz. (3,000 gm.). The rectum was repaired, and he was discharged weighing 7 lb. 3 oz. (3,300 gm.) and in excellent physical condition.

A second admission occurred five weeks later because of failure to gain and a diarrhea of two days' duration. There was no vomiting. Hydration and nutrition were poor, the weight being 7 lb. 2½ oz. (3,250 gm.). Urinalysis and stool examinations showed nothing abnormal. The blood count was normal.

There was no response to formula changes, and in spite of parenteral administration of fluids and blood, plasma, and antibiotics, his weight decreased to 6 lb. during the next seven days. At this time, the carbon dioxide combining power was 30.5 mEq. per liter and the blood chlorides were 100 mEq. per liter. The eosinophile count was 275. Administration of desoxycorticosterone acetate, 2.5 mg., and sodium chloride, 1 gm., daily was started and continued for 13 days; then these were given three times a week for one week and two times a week for another week. The patient gained 1 lb. 13 oz. (810 gm.) in 13 days, and at the end of this therapy his weight was 8 lb. (3,630 gm.). Four days after this therapy was begun the carbon dioxide combining power had increased to 33.5 mEq. per liter and the chlorides to 118.4 mEq. per liter. The pH was 7.4. One week after the start of therapy the eosinophile count was 362.5. Four days after therapy was stopped, the combining power of the carbon dioxide was 25 mEq. per liter and the chlorides were 128.2 mEq. per liter, with a pH of 7.4.

This patient was admitted for a third time on Oct. 18 with signs of intestinal obstruction. At operation several adhesions were found and severed. Recovery was rapid. The weight at this time was 9 lb. 4 oz. (4,200 gm.).

This infant gained 2 lb. during 23 days of desoxycorticosterone acetate and sodium chloride therapy after a failure to respond to other forms of treatment. There were a rapid correction of the diarrhea and improvement in the appetite.

CASE 9.—P. B., a 4½-month-old white boy, was admitted to the Children's Memorial Hospital on Sept. 11, 1950, with a history of diarrhea and vomiting of five days' duration. The birth weight was 7 lb. (3,200 gm.); the admission weight was 10 lb. 14 oz. (4,900 gm.). The infant was pale, moderately malnourished, and dehydrated. The blood count, serologic study, and urinalysis showed no abnormalities. The nonprotein nitrogen was 26 mg. per 100 cc. Administration of fluids intravenously and of blood, plasma, vitamins, antibiotics, and various formulas was done.

The infant did poorly and on Sept. 29 weighed only 9 lb. 11 oz. (4,400 gm.). At this time the carbon dioxide combining power was 20 mEq. per liter, the serum potassium was 9.7 mEq.

per liter, and the serum chlorides were 165 mEq. per liter. The eosinophile count was 18.75. Administration of desoxycorticosterone acetate, 2.5 mg., and sodium chloride, 1 gm., was started, and this was continued until Oct. 6, at which time the same dose was given there times weekly until Oct. 11, and then twice weekly until Oct. 16. At this time the weight was 11 lb. 6 oz. (5,200 gm.). On Oct. 9 the serum potassium was 3.5 mEq. per liter. The eosinophile count on Oct. 13 was 68.75.

On the desoxycorticosterone acetate therapy this infant gained 1 lb. 11 oz. (770 gm.) in 16 days. He immediately began to eat well, and the diarrhea subsided. On discharge Oct. 25 the weight was 12 lb. 1½ oz. (5,500 gm.), and he has continued to do well.

CASE 10.—A. S., a 4-month-old white boy, was admitted to the Children's Memorial Hospital on Sept. 6, 1950, with a history of vomiting and diarrhea of two days' duration. The birth weight was 6 lb. 6½ oz. (2,850 gm.); the admission weight was 9½ lb. (4,300 gm.). He had been admitted previously for a steatorrhea and was being fed on a celiac diet. A sibling has fibrocystic disease of the pancreas. On examination there were malnutrition, severe dehydration, grey-blue color, sunken eyes, respiration rate of 10 a minute, and pulse rate of 60 to 80 a minute. Blood count, urinalysis, chest roentgenogram, cardiac fluoroscopy and stool cultures showed normal results. The Mantoux reaction was negative. The vitamin A curve was flat. Trypsin digestion of the x-ray film by the stool was positive. The electrocardiogram was compatible with hypopotassemia. The carbon dioxide combining power was 20 mEq. per liter. On Sept. 20, the serum sodium was 147 mEq. per liter, the potassium was 11.9 mEq. per liter, the nonprotein nitrogen was 38 mg. per 100 cc. and the chlorides were 122.9 mEq. per liter. On Sept. 26 the serum potassium was 10.5 mEq. per liter. The eosinophile count on Sept. 30 was 271.25.

Therapy consisted in administration of fluids intravenously, plasma, blood, vitamins, calcium gluconate, nikethamide, caffeine, oxygen, antibiotics, whole adrenal cortical extract, and fluids and adequate formulas by mouth. The high potassium value can possibly be explained by the fact that larger than normal amounts of Darrow's solution were administered within the first 24 hours. During the three weeks of the above therapy there was a 4 oz. (113 gm.) weight gain.

On Sept. 30 the weight was 9 lb. 12 oz. (4,420 gm.). Daily administration of desoxycorticosterone acetate 2.5 mg. and sodium chloride 1 gm. was started and continued to Oct. 16, at which time he weighed 11 lb. 3 oz. (5,100 gm.). The eosinophile count on Oct. 9 was 193.75. On Oct. 13 the serum potassium was 6.8 mEq. per liter. He then failed to gain and was again given desoxycorticosterone acetate and sodium chloride, as before, on Oct. 22, and the therapy was continued until Oct. 26. The weight on Oct. 22 was 11 lb. 1 oz. (5,000 gm.). He began to improve again and was discharged on Nov. 8 weighing 11 lb. 9 oz. (5,240 gm.).

Taking into consideration the extreme lability of celiac disease, this patient showed marked clinical improvement and a gain of 1 lb. 6 oz. (620 gm.) in 16 days on desoxycorticosterone acetate and sodium chloride therapy after three weeks of orthodox therapy.

## COMMENT

Dehydration and malnutrition are frequently seen associated with vomiting and diarrhea in infants. Most patients respond well to administration of fluids parenterally, plasma, blood, and antibiotics. However, occasionally some of these infants are refractory to the standard therapeutic regimens. Ten such patients have been described who were treated with desoxycorticosterone acetate and sodium chloride. Two of these infants appeared clinically to represent evidence of adrenal cortical failure.

Jaudon [3] has stated that such temporary adrenal dysfunction can occur during infancy and that boys are usually affected. Blood chemistry determinations may reveal normal to depressed sodium and depressed chloride and carbon dioxide combining power. Nonprotein nitrogen and potassium may be elevated.

Of the group of patients described here, eight of the 10 were boys. Nine of the 10 patients were under 6 months of age, and one was 1 year of age.

Blood chemistry levels in our series were as follows: sodium determinations in three of the 10 cases showed normal levels; chloride determinations in seven of the 10 cases revealed five normal levels, one elevation, and one depression. Potassium determinations in three of the 10 cases showed all elevated levels. (In Case 10, however, there were electrocardiographic and clinical findings of hypopotassemia. One must bear in mind that the electrocardiogram is a better determinant of this intracellular cation than the chemical serum determinations of potassium from the extracellular fluid compartment.) The carbon dioxide combining power, determined in seven of the 10 cases, was normal in one case, low normal in two cases, depressed in two cases, and elevated in two cases. Nonprotein nitrogen determinations in four cases showed normal levels. The results of these chemistry studies were, in general, not consistent with adrenal cortical hypofunction. There was no correlation between the clinical picture and total eosinophile response in three of the 10 cases in which such determinations were made.

When improvement took place, it was usually striking. There were cessation of vomiting and diarrhea and improvement in appetite. The infants became hungry. In all infants there was some evidence of edema which was slight in all but one case. Treatment was stopped because of this in only one case (Case 6). When administration of desoxycorticosterone acetate and sodium chloride was stopped, there was usually a loss in weight of several ounces within 24 to 48 hours, after which a steady but normal weight gain took place. Just how much the retention of fluid means in these cases has not been determined. We have given sodium chloride, 1 to 2 gm., daily to a few infants without the addition of desoxycorticosterone acetate and have not had the same results as when the two were combined.

Weight gain and clinical improvement were noted in nine of the 10 cases. It appears that this treatment may be indicated for infants who fail to respond to standard therapeutic measures whether or not they present evidence of adrenal cortical failure.

## SUMMARY

Ten cases of dehydration and malnutrition in infants treated with desoxycorticosterone acetate and sodium chloride have been presented. Of this number, only two cases appeared clinically to represent evidence of adrenal cortical hypofunction causing disturbances of mineral metabolism.

Therapeutic response to desoxycorticosterone acetate and salt was dramatic in all but one case (Case 7). This patient was markedly dehydrated after a colostomy for agenesis of the myenteric plexus and failed to respond to all treatment.

From the above clinical results, further observation of treatment with desoxycorticosterone acetate and sodium chloride may be indicated in malnourished and dehydrated infants who have failed to respond to the standard types of management. It must be emphasized that this is purely an empirical method of treatment. The exact role that the adrenal gland plays in these patients is not known. Patients receiving desoxycorticosterone acetate should be watched very carefully for the development of edema.

# BLOOD LEVEL OF THIAMINE IN NORMAL CHILDREN

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A DIRECT approach to the evaluation of nutritional status by quantitatively determining levels of specific nutritional factors in body tissues and fluids is receiving increasing attention. Darby [1] has recently emphasized the desirability of obtaining laboratory studies to support the clinical evaluation, and Jolliffe, Tisdall, and Cannon [2] have emphasized the need for specific information on blood levels of the vitamins of the B group. Therefore, we decided to accumulate data on thiamine by direct blood-level determination when an opportunity to study healthy children presented itself. We believe such data to be desirable to supplement information obtained from a variety of techniques, including clinical assessment of the patient, excretion studies of carbohydrate metabolites, and electrocardiographic determinations, all of which may reflect thiamine nutrition indirectly. A recent review of vitamin requirements in adolescence [3] further emphasized the relative paucity of information on thiamine requirements during growth.

## MATERIAL AND METHODS

Approximately 15 ml. of blood were withdrawn from all patients prior to the morning meal and placed in a sterile bottle which contained dry ammonium and potassium oxalates. The blood was mixed, kept refrigerated, and brought to the laboratory for analysis. Thiamine was determined on whole blood according to the modified method of Friedemann and Kmieciak.[4] While it is recognized that the majority of the thiamine is in the red blood cells, determinations on whole blood are valid, since all the children studied had hematocrit values within the normal range. Suitable internal and external standards were used, and recovery experiments were done concurrently in order to maintain uniformity of the absorption technique. Determinations made on stored samples indicated little or no loss within a two-week period. At least one blood thiamine determination was performed on each child, and many had additional determinations done at intervals.

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From the Department of Pediatrics, University of Illinois College of Medicine.

1. Darby, W. J.: Evaluation of the Symptoms and Signs of Deficiency Diseases, Federation Proc. **9**:592 (Sept.) 1950.

2. Jolliffe, N.; Tisdall, F. F., and Cannon, P. R.: Clinical Nutrition, New York, Paul B. Hoeber, Inc., 1950.

3. Waisman, H. A.; Richmond, J. B., and Williams, S. J.: Vitamin Requirements in Adolescence, J. Pediat. **37**:922 (Dec.) 1950.

4. Friedemann, T. E., and Kmieciak, T. C.: The Determination of Thiamine in Blood, J. Lab. & Clin. Med. **28**:1262 (July) 1943.

The thiamine determinations were made on two groups of children. The first group comprised 54 children varying in age from 8 to 17 years selected from the outpatient department and from the pediatric ward of the University of Illinois Research and Educational Hospitals. These children were living at home, and during the time they were observed no attempt was made to modify their dietary patterns.

The second group consisted of 214 presumably healthy children ranging in age from 6 to 20 years who lived in an institution in which they were grouped in cottages under the supervision of cottage parents. All of the children were offered identical diets from a central kitchen at all times.

TABLE 1.—*Thiamine Level of Blood in Normal Noninstitutional Children*

| | Range of Thiamine in Blood (γ per 100 Cc.), No. of Children | | | | | | | | | | | | | Thiamine Level of Blood, γ per 100 Cc. | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Age, Yr. | 4-5 | 5-6 | 6-7 | 7-8 | 8-9 | 9-10 | 10-11 | 11-12 | 12-13 | 13-14 | 14-15 | 15-16 | 16-17 | Total | Range | Mean | S. D.* |
| **Boys** | | | | | | | | | | | | | | | | | |
| 6-10 | .. | .. | 1 | 3 | 2 | .. | .. | .. | .. | .. | 1 | .. | .. | 7 | 7.0-15.0 | 8.33 | 2.80 |
| 11-15 | 2 | 3 | 1 | 2 | 3 | 3 | 1 | 1 | 1 | .. | .. | .. | .. | 17 | 4.8-12.4 | 8.19 | 2.44 |
| 16-20 | .. | .. | .. | .. | .. | 1 | .. | .. | 1 | .. | .. | .. | .. | 2 | 10.0-12.0 | 11.10 | .... |
| Total | 2 | 3 | 2 | 5 | 5 | 4 | 1 | 1 | 2 | .. | 1 | .. | .. | 26 | 4.8-15.0 | 8.55 | 2.53 |
| **Girls** | | | | | | | | | | | | | | | | | |
| 6-10 | 1 | 1 | 2 | 2 | .. | .. | .. | 1 | .. | 1 | 1 | .. | .. | 9 | 5.0-15.0 | 8.87 | 3.58 |
| 11-15 | 1 | .. | 2 | 3 | 3 | 4 | .. | 3 | 1 | 1 | .. | .. | 1 | 19 | 5.0-17.0 | 9.64 | 2.86 |
| Total | 2 | 1 | 4 | 5 | 3 | 4 | .. | 4 | 1 | 2 | 1 | .. | 1 | 28 | 5.0-17.0 | 9.35 | 3.06 |
| Total boys and girls | 4 | 4 | 6 | 10 | 8 | 8 | 1 | 5 | 3 | 2 | 2 | .. | 1 | 54 | 4.8-17.0 | 9.00 | 2.82 |

* Standard deviation.

TABLE 2.—*Thiamine Level of Blood in Normal Institutional Children*

| | Range of Thiamine in Blood (γ per 100 Cc.), No. of Children | | | | | | | | | | | | Thiamine Level of Blood, γ per 100 Cc. | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Age, Yr. | 5-6 | 6-7 | 7-8 | 8-9 | 9-10 | 10-11 | 11-12 | 12-13 | 13-14 | 14-15 | 15-16 | Total | Range | Mean | S. D.* |
| **Boys** | | | | | | | | | | | | | | | |
| 6-10 | .. | .. | .. | 3 | 9 | 7 | 8 | 9 | 2 | .. | 1 | 39 | 8.33-15.42 | 11.09 | 1.50 |
| 11-15 | .. | .. | 1 | 6 | 10 | 10 | 14 | 14 | 2 | 3 | .. | 60 | 7.92-15.00 | 11.15 | 1.52 |
| 16-20 | .. | .. | 1 | .. | 6 | 7 | 6 | 2 | .. | .. | .. | 22 | 7.08-12.50 | 10.57 | 1.24 |
| Total | .. | .. | 2 | 9 | 25 | 24 | 28 | 25 | 4 | 3 | 1 | 121 | 7.08-15.42 | 11.02 | 1.48 |
| **Girls** | | | | | | | | | | | | | | | |
| 6-10 | .. | .. | .. | 2 | 4 | 1 | 7 | 3 | .. | .. | .. | 17 | 8.75-12.92 | 10.96 | 1.23 |
| 11-15 | 1 | 1 | 2 | 1 | 13 | 13 | 15 | 7 | .. | .. | 1 | 54 | 5.25-15.42 | 10.69 | 1.64 |
| 16-20 | .. | .. | .. | 2 | 2 | 2 | 6 | 7 | 2 | 1 | .. | 22 | 8.33-14.17 | 11.48 | 1.50 |
| Total | 1 | 1 | 2 | 5 | 19 | 16 | 28 | 17 | 2 | 1 | 1 | 93 | 5.25-15.42 | 10.96 | 1.56 |
| Total boys and girls | 1 | 1 | 4 | 14 | 44 | 40 | 56 | 42 | 6 | 4 | 2 | 214 | 5.25-15.42 | 10.96 | 1.51 |

* Standard deviation.

An attempt was made to obtain a rough correlation of the caloric intake with the calculated thiamine in the diet. It has been shown that the need for thiamine is directly related to the carbohydrate utilized [5]; therefore, since no estimate could be made from the diet of the children living at home, we felt that the more reliable calculations could be made from the planned menus furnished the institutional children. It was calculated that the average daily planned diet

5. Cowgill, G. R.: Vitamin B Requirement of Man, New Haven, Yale University Press, 1934. Williams, R. R., and Spies, T. D.: Vitamin $B_1$ (Thiamin) and Its Uses in Medicine, New York, The Macmillan Company, 1938. Jolliffe, N.: New International Clinics, Philadelphia, J. B. Lippincott Company, Series 48, Vol. 10, 1938.

in the institution provided approximately 2,400 Cal. and 1.5 mg. of thiamine. This menu furnished 0.63 mg. of thiamine per 1,000 Cal.

## RESULTS

The results of the study of the thiamine level in the blood of normal children who were observed in the outpatient department and hospital ward are presented in Table 1. The range of thiamine values are listed in micrograms per 100 cc. in increments of 1 γ according to the patient's age. It may be noted that most of the patients in the 6 to 10 year age group had values which were between 6 and 9 γ per 100 cc. In the 11 to 15 year age group most of the values were within the same range but revealed a slightly greater spread of the values. In general there was no great difference between boys and girls, and if one contrasts the mean for the different age groups, the values are reasonably close.

The thiamine blood levels of healthy children in the institutional environment are presented in Table 2. In this larger group of children it will be seen that the mean values are more uniform and that there is little difference between the sexes. When the data from all boys are averaged, the value is 11.02 γ, and this compares closely with 10.93 for all girls. It is of interest that about 90% of the figures are between 8.0 and 13.0 γ, with an average of 11.0 γ.

## COMMENT

The data available in the literature on thiamine blood levels of normal children are summarized in Table 3. It should be noted that a variety of methods were used to evaluate the thiamine content of blood. In general, the range is that which might be expected on the basis of the different methods used.

In order to assess the influence of age on blood thiamine levels, a comparison of the figures obtained from studies of children with those obtained on adults can be made only after critical appraisal of the available data obtained by a variety of methods. The pertinent data on adults available in the literature are presented in Table 4. The values were slightly below those found in children, but many of the blood thiamine determinations in these studies were done by fermentation methods.

One way of establishing the daily thiamine requirement is to relate it to the total carbohydrate intake, since the vitamin is part of the coenzyme cocarboxylase concerned in carbohydrate metabolism. Other workers have attempted to relate this requirement to the blood thiamine level in persons who received diets of known thiamine intake. The work of Oldham and co-workers [6] demonstrated that a blood level of thiamine was 5.2 γ per 100 cc. on an ordinary diet but dropped to 3.8 γ after the intake of thiamine was reduced to 0.29 mg. a day for a 59-day period. The blood level rose again to 5.3 γ per 100 cc. after the intake of thiamine was again increased. Similarly, the work of Friedemann and co-workers [7] showed that the level of 6.59 γ per 100 cc. on intake of 0.85 mg. a day was raised to 7.85 γ when the thiamine intake was increased to 2.37 mg. a day. Additional confirmatory work by

6. Oldham, H. G.; Davis, M. V., and Roberts, L. J.: Thiamine Excretions and Blood Levels of Young Women on Diets Containing Varying Levels of the B Vitamins, with Some Observations on Niacin and Pantothenic Acid, J. Nutrition **32**:163 (Aug.) 1946.

7. Friedemann, T. E.; Ivy, A. C.; Jung, F. T.; Sheft, B. B., and Kinney, V. M.: Work at High Altitude: Utilization of Thiamine and Riboflavin at Low and High Dietary Intake; Effect of Work and Rest, Quart. Bull. Northwestern M. School **23**:177, 1949.

Oldham and co-workers [8] showed that after three to eight weeks the children who received a daily intake of 0.45 to 0.6 mg. of thiamine had a blood level of 5.5 γ per 100 cc. When the diet was improved so that it contained 1.1 to 1.4 mg. of thiamine a day for a period of four weeks, the blood value increased to 7.3 γ per 100 cc. One

TABLE 3.—*Data on Blood Thiamine Level in Normal Children from Other Authors*

| Method | Author | Age | Sex | No. of Cases | Daily Intake of Thiamine, Mg. | Thiamine Level of Blood, γ per 100 Cc. | |
|---|---|---|---|---|---|---|---|
| | | | | | | Range | Mean |
| Cocarboxylase | Goodhart [9] | 5-15 yr. | M | 28 | ..... | 4.0-10.0 | 7.0 ± 1.53 |
| Cocarboxylase | Wortis, H.; Goodhart, R. S., and Bueding, E.: Am. J. Dis. Child. 61:226 (Feb.) 1941 | Below 12 yr.<br>Above 12 yr. | ..<br>.. | 26<br>24 | .....<br>..... | 4.0-13.0<br>4.0-13.0— | 8.0 ± 2.06<br>6.5 ± 1.88 |
| Cocarboxylase | Schultz, F. W., and Knott, E. M.: Am. J. Dis. Child. 61:231 (Feb.) 1941 | Below 1 yr. | .. | 12 | ..... | 6.7-16.5 | 10.0 up |
| Thiochrome.... | Benson and co-workers [12] | 4-12 yr. | M<br>F | 22<br>23 | 0.63-1.11 | 4.8-12.3 | 7.8 ± 1.3 |
| Fermentation | Oldham and co-workers [8] | 6-15 yr. | .. | 39 | 0.46-0.6 (3-8 wk.) | ..... | 5.5 |
| | | | | 40 | 1.1-1.4 (4 mo.) | ..... | 7.3 |
| Thiochrome | Slobody, L. B.; Willner, M. M., and Mestern, J.: Am. J. Dis. Child. 77:736 (June) 1949 | 5 days | .. | 85 | ..... | 2.08-15.8 | 9.57 |

TABLE 4.—*Data on Thiamine Level of Blood in Adults from Other Authors*

| Method | Author | Age, Yr. | Sex | No. of Cases | Daily Intake of Thiamine, Mg. | Thiamine of Blood, γ per 100 Cc. | |
|---|---|---|---|---|---|---|---|
| | | | | | | Range | Mean |
| Phycomyces | Rowland, E. N., and Wilkinson, J. F.: Brit. M. J. 2:878 (Oct. 29) 1938 | Adult | F<br>M | 2<br>6 | .....<br>..... | 6.5-16.5 | 10.4 |
| Phycomyces | Lehmann, J., and Nielsen, H. E.: Acta med. scandinav. 99:577, 1939 | Adult | F<br>M | 10<br>36 | .....<br>..... | 8.0-12.0<br>7.0-13.0 | 9.0 |
| Phycomyces | Sinclair, H. M.: Biochem. J. 33:2027 (Dec.) 1939 | Adult | .. | 45 | ..... | 5.5-10.5 | 7.4 |
| Cocarboxylase | Goodhart [10a] | 20-40 | M | 26 | ..... | 4.5-12.0 | 7.0 |
| Fermentation | Goodhart [10b] | Adult | .. | 45 | ..... | 3.1-9.2 | 5.39 |
| Thiochrome | Friedemann and Kmieciak [4] | Adult | M<br>F | 29<br>7 | .....<br>..... | 3.8-11.2<br>3.0-9.2 | 5.73<br>5.60 |
| Phycomyces | Bang [11] | 19-70 | M<br>F | 18<br>20 | .....<br>..... | 5.7-11.5 | 7.9 |
| Fermentation | Oldham and co-workers [6] | 19-32 | F | 11<br>9<br>9<br>5<br>6 | Ordinary diet<br>0.29 (59 days)<br>0.40 (47 days)<br>0.70 (45 days)<br>0.90 (41 days) | 4.0-6.7<br>2.6-5.0<br>4.3-6.7<br>6.0-7.2<br>5.4-6.4 | 5.2<br>3.8<br>5.3<br>6.8<br>5.6 |
| Thiochrome | Kirk, E., and Chieffi, M.: J. Nutrition 38:353 (July) 1949 | 16-39<br>40-59<br>60-69<br>70-79<br>Above 80 | ..<br>..<br>..<br>..<br>.. | 29<br>42<br>48<br>71<br>59 | 1.9<br>1.9<br>1.9<br>1.9<br>1.9 | 2.0-5.5<br>1.2-6.3<br>0.7-7.2<br>0.8-7.2<br>0.6-6.5 | 3.8<br>3.3<br>3.7<br>3.2<br>3.1 |
| Thiochrome | Friedemann and co-workers [7] | 22-27 | M | 6<br>5<br>7<br>3 | 0.85<br>2.37<br>2.77<br>3.06 | 5.0-11.0 | 6.59<br>7.85<br>9.37<br>9.04 |

consideration which must be kept in mind is that whenever the intake of bread and other cereals is increased, they will contribute thiamine as well as calories, because of the program of flour and cereal enrichment now existing in the majority of states in this country.

8. Oldham, H. G.; Roberts, L. J., and Young, M.: Results of Providing a Liberally Adequate Diet to Children in an Institution: Blood and Urinary Excretion Studies Before and After Dietary Improvement, J. Pediat. **27**:418 (Nov.) 1945.

The thiamine blood determinations in the group of children seen in a pediatric outpatient population furnished values for patients receiving home care for whom no special attempt at improving nutrition was made. In the second group of subjects living at the children's school a calculation of the caloric intake as well as the thiamine intake was possible, using known figures for thiamine in the foods consumed. It was reognized that the calculation did not account for variations in intake or destruction by cooking procedures but merely provided a means by which one could appraise the blood thiamine level in children exposed to an adequate diet. While it was not possible to determine the thiamine intake in the children living at home, an estimate of the intake by the children in the institution was found to average 1.5 mg. a day for children of various ages. This was within the minimum range for girls and for boys recommended by the Committee on Foods of the National Research Council in 1948.

The finding that the blood thiamine values of the children fed the institutional diet were in the same range as those of the children cared for at home is of interest. Since the difficulties inherent in any large quantity cookery may predispose to destruction of vitamins, blood levels attained by the institutional children would indicate that the dietary is as adequate so far as thiamine is concerned as that received by the children residing at home. The slightly higher average and narrower range of values for the institutional children may be a reflection of planned menus. It may be presumed, therefore, that the blood values reported in this study are average values for normal children.

The consensus regarding the influence of age on the thiamine in the blood is that insignificant differences can be found between adults and children. Goodhart [9] and Goodhart and Sinclair,[10] for example, and Bang,[11] as well as Benson and associates,[12] found no difference in blood levels in the various age groups. These workers explained that the entire blood chemistry of the child was not significantly different from that of the adult, and it would be unrealistic to expect that the thiamine level would be different. The figures reported in this paper show that no differences were found in the various age groups from 6 to 20 years.

It is generally agreed that the thiamine in the blood remains relatively stationary over a short depletion period and does not immediately reflect wide fluctuations in thiamine intake. The blood thiamine may provide a very definite reservoir from which various tissues can obtain the vitamin as it is needed in enzymatic processes concerned with carbohydrate breakdown, and it may be that a fall in the blood values will reflect only gross tissue depletion. This has a parallel in the relation between ascorbic acid values in the plasma and in the tissues. Ascorbic acid deficiency is

9. Goodhart, R.: A Revaluation of the Method Described by Goodhart and Sinclair for the Determination of Blood Cocarboxylase Values, J. Biol. Chem. **135**:77 (Aug.) 1940.

10. (*a*) Goodhart, R. S., and Sinclair, H. M.: The Estimation of Cocarboxylase (Vitamin $B_1$ Diphosphate Ester) in Blood, Biochem. J. **33**:1099 (July) 1939. (*b*) Goodhart, R., and Nitzberg, T.: The Thiamine Content of Human Blood and Urine as Determined by Fermentation Method, J. Clin. Invest. **20**:625 (Nov.) 1941.

11. Bang, H. O.: Determination of Vitamin $B_1$ in the Blood from Healthy and Diseased Persons: Phycomyces Method, Acta med. scandinav. **122**:38, 1945.

12. Benson, R. A.; Slobody, L. B.; Witzberger, C. M., and Lewis, L.: The Blood Level of Vitamin $B_1$ in Healthy Children and Its Relation to the Urinary Thiamine, J. Pediat. **21**:659 (Nov.) 1942.

reflected by a decrease in plasma levels long before tissue undersaturation develops. Abnormally low levels of blood thiamine may thus be of some clinical value as an indirect assessment of thiamine tissue status.

## SUMMARY AND CONCLUSIONS

Fifty-four normal children in a pediatric outpatient department fed apparently adequate diets at home showed whole-blood thiamine values ranging from 4.8 to 17.0 γ per 100 cc., with a mean of 9.0 ± 2.82. The thiamine blood levels of 214 normal healthy children cared for in an institution and receiving planned menus showed a range of 5.25 to 15.42 γ per 100 cc. of blood, with a mean of 10.98 ± 1.51. Age seemed to have no significant influence on the range of values obtained.

Dr. Herbert Grossman aided in gathering many of the blood samples.

Dr. Gerald M. Cline, Medical Director of the Illinois Soldier's & Sailor's Children's School, Normal, Ill., and the staff of the institution gave cooperation in this study.

# ARTERIOSCLEROSIS IN INFANCY

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THIS PAPER presents the clinical and pathological findings of generalized arteriosclerosis occurring in a 5-month-old infant. The baby died of myocardial infarction which resulted from multiple coronary occlusions. Since the first case report by Bryant and White,[1] in 1891, additional reports have appeared in the domestic and foreign literature.[2]

## REPORT OF A CASE

A 5-month-old white boy was admitted to the Jewish Hospital, Philadelphia, on July 8, 1947, with a chief complaint of cough of three months' duration. The baby had progressed satisfactorily until the age of 8 weeks, when a persistent cough and anorexia developed. Three days before admission the cough became worse, and there was marked irritability. A low-grade fever had been present for one week. In the two months prior to admission there was a 480-gm. weight loss. His vitamin intake was adequate. His mother had rheumatic fever in childhood; however, her pregnancy was uneventful, and the baby was delivered spontaneously at term with no neonatal complications. The remainder of the family history was noncontributory.

Physical examination revealed a pale, dyspneic, cyanotic, irritable, and malnourished infant who was crying and coughing incessantly. The baby was moderately dehydrated. The rectal temperature was 40 C. (104 F.), and the pulse rate was 160. Accurate blood pressure readings

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From the Pediatric Department, Jewish Hospital.

1. Bryant, J. H., and White, W. H.: A Case of Calcification of the Arteries and Obliterative Endarteritis, Associated with Hydronephrosis, in a Child Aged 6 Months, Guy's Hosp. Rep. **32**:17-28, 1891.

2. (*a*) Ramsay, R. E., and Crumrine, R. M.: Coronary Thrombosis in an Infant Aged 4 Months, Am. J. Dis. Child. **42**:107-110 (July) 1931. (*b*) Lightwood, R.: A Case of Dwarfism and Calcinosis Associated with Widespread Arterial Degeneration, Arch. Dis. Childhood **7**:193-208, 1932. (*c*) Oppenheimer, E. H.: Partial Atresia of the Main Branches of the Pulmonary Artery Occurring in Infancy and Accompanied by Calcification of the Pulmonary Artery and Aorta, Bull. Johns Hopkins Hosp. **63**:261-277, 1938. (*d*) Ross, S. G., and Williams, W. E.: Vitamin D Intoxication in Infancy, Am. J. Dis. Child. **58**:1142 (Nov.) 1938. (*e*) van Creveld, S.: Coronary Calcification and Thrombosis in an Infant, Ann. Pædiat. **157**:84-92, 1941. (*f*) Baggenstoss, A. M., and Keith, H. M.: Calcification of the Arteries of an Infant: Report of a Case, J. Pediat. **18**:95-102, 1941. (*g*) Scott, E. P., and Miller, A. J.: Coronary Thrombosis: Report of a Case in an Infant 11-Months of Age, ibid. **28**:478-480, 1946. (*h*) Brown, C. E., and Richter, I. M.: Medial Coronary Sclerosis in Infancy, Arch. Path. **31**:449-457 1941. (*i*) Stryker, W. A.: Coronary Occlusive Disease in Infants and in Children, Am. J. Dis. Child. **71**:280-300 (March) 1946. (*j*) Field, M. H.: Medial Calcification of Arteries of Infants, Arch. Path. **42**:607-618 (Dec.) 1946. (*k*) Ravich, R. N., and Rosenblatt, S.: Myocardial Infarction in the Newborn Infant, J. Pediat. **29**:266-273, 1947. (*l*) Stryker, W. A.: Arterial Calcification in Infancy with Special Reference to the Coronary Arteries, Am. J. Path. **22**:1007-1031, 1946.

could not be obtained. Other pertinent findings were limited to the thorax. There were retractions of the intercostal spaces with inspirations. A precordial bulge was noted. There was dulness on percussion throughout the entire left hemithorax, with decreased breath sounds over the same area. The heart sounds were faint, and there were no thrills or murmurs. The cardiac apex was located in the fifth left interspace at the anterior axillary line. The patient died before an eyeground examination was done.

Preliminary diagnoses were (1) pericardial effusion; (2) anomalous origin of the left coronary artery from the pulmonary artery, and (3) congenital heart disease with congestive failure.

*Clinical Course.*—After temporary improvement in an oxygen tent the dyspnea increased. A chest roentgenogram confirmed the presence of pericardial effusion (Fig. 1). A pericardial

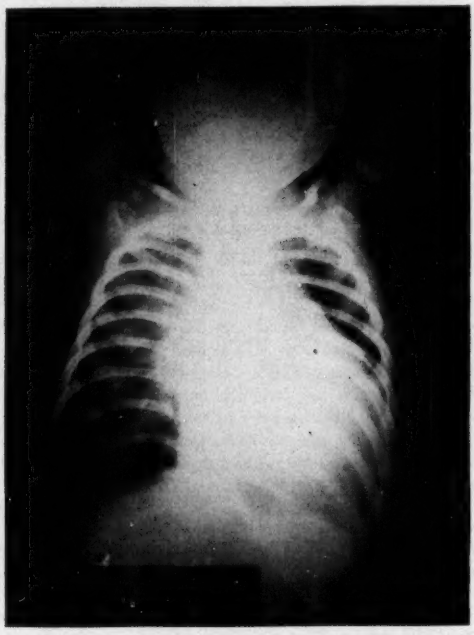

Fig. 1.—Cardiac dilation; a small amount of pericardial fluid was also present.

tap yielded 25 cc. of yellow fluid. Only slight relief followed this procedure. The following day the dyspnea became more marked, and the baby died 36 hours after admission.

The laboratory findings included a hypochromic, normocytic anemia, a normal white blood cell count, a negative serological reaction for syphilis, and a negative urinalysis. The blood culture and pericardial-fluid cultures were negative.

The electrocardiogram (Fig. 2) was strongly suggestive of coronary artery disease with myocardial damage.

*Autopsy Report.*—The autopsy was performed 12 hours after death. The pertinent findings were the following:

Gross Pathology: The right pleural cavity contained 50 cc. of straw-colored fluid; the left pleural cavity was occupied in its lower half by the dilated heart which compressed the left lung. The pericardial sac contained a slight excess of clear fluid, and the pericardium was markedly congested. The liver extended 5 cm. below the right costal border in the midclavicular line. There were no anomalies of the great vessels. The heart weighed 100 gm. (normal 40

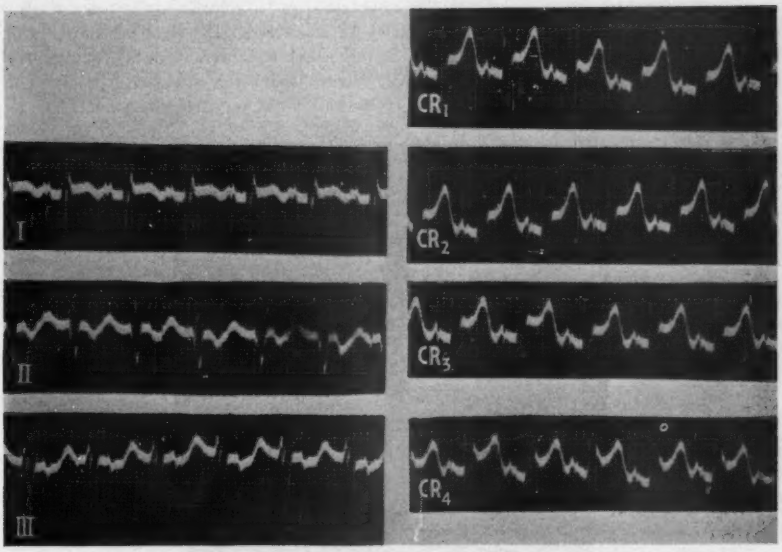


Fig. 2.—The electrocardiogram shows sinus tachycardia of 158 with right axis deviation. There is an elevated ST segment with an inverted T wave ("cove-shaped" complex) with prominent Q wave in lead I. The T waves are inverted in leads II and III with depressed ST segment in lead III. The chest leads all show elevated ST segments and prominent upright T waves.

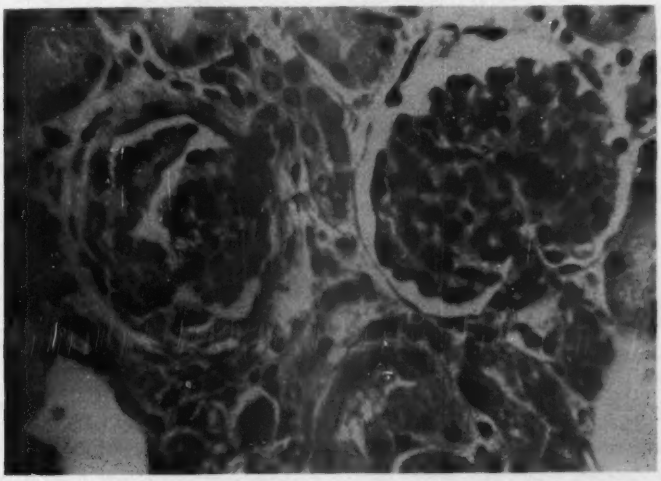

Fig. 3.—Two glomeruli of the left kidney. The right glomerulus is normal; the left glomerulus shows fibrosis and hyalinization. High power; trichrome stain.

gm.) and was enormously dilated. The left ventricular wall measured 1 cm. at its base, and its inner portion was white and firm and composed of fibrous tissue, in contrast to the dark red color of the muscular outer portion. The endocardium was thickened. The right ventricular wall was 3 to 4 mm. in thickness, with no areas of fibrosis. Both atria were dilated. The coronary arteries were very narrow, with scarcely visible lumens, and barely admitted a probe. The intima was smooth. The branches were small, thick-walled, and very difficult to trace.

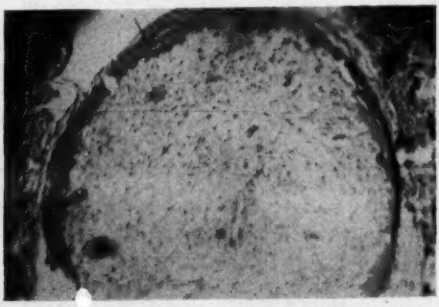

Fig. 4.—Renal arteriole, showing endothelial proliferation and hyaline deposition in the intima (low power).

Fig. 5.—Descending branch of the right coronary artery, showing marked intimal proliferation, narrowing of the lumen, and a localized area of degeneration and calcification. Low power; hematoxylin-eosin stain.

The right lung weighed 100 gm. and showed compensatory emphysema, except posteriorly, where it was atelectatic. The left lung weighed 60 gm. It was compressed by the heart and was completely atelectatic.

The remaining organs were grossly normal. Permission was not secured for examination of the brain.

Microscopic Pathology: Extensive changes were found in the heart. Sections of the apex of the left ventricle showed that a large portion of the muscle had been replaced by fibrous tissue. There was one small area where the muscle fibers had been directly impregnated with

calcium salts. The remaining muscle fibers were hypertrophied. Among these fibers and in the fibrous tissue were many large blood sinuses. The interventricular septum also showed extensive fibrosis. The greater part of the kidney tissue was intact, but beneath the capsule were a number of glomeruli in various stages of degeneration (Fig. 3). Many of the afferent arterioles were narrow owing to endothelial proliferation and hyaline deposition in the intima (Fig. 4).

The primary disease was located in the arterial system and chiefly in the small muscular arteries. The most striking lesion was the narrowing of the arterial lumen by intimal proliferation even to the point of complete occlusion. Almost as striking were the varying degrees of degeneration and calcification found in the media and intima. In a few vessels foreign-body giant cells were seen. The internal elastic lamina was frequently fragmented, and often calcium was laid down contiguous to it. In other areas, degeneration and calcification appeared in the elastic lamina. Extensive lesions were present in the coronary arteries (Fig. 5), renal arteries and arterioles, and arteries of the periadrenal fat. The earliest stages of the lesions were found in a few of the small pulmonary arterioles. These showed intimal necrosis and vacuolization between the endothelium and the internal elastic lamina. In these areas there were granular material surrounded by a few fine fibers and scattered large nuclei of histiocytes and monocytes.

## COMMENT

In generalized arteriosclerosis in infants, arterial occlusion is the end result of a characteristic pathological pattern. The arterial lesions have been described as essentially a calcification of the media and internal lamina and a fibroblastic proliferation of the intima. The medium-sized and small arteries have been most frequently affected. In our case the earliest arterial lesions are those of necrosis and exudation followed by granulomatous proliferation. The exudation is seen more in the intima, and the necrosis, in the internal elastic lamina and media. The subsequent calcification of the lesions is not a process which differs from calcification elsewhere, and its primary requisite, necrotic tissue, is found in abundance in the vessel wall.

The etiology of this disease is unknown. There has been no demonstrable evidence of an infective agent. Attempts to explain this condition by reference to a disturbance in calcium metabolism have been similarly fruitless. Field [21] discussed this problem in detail and was unable to explain it on the basis of vitamin D poisoning, hyperparathyroidism, or other disturbances of calcium metabolism. While allergy has been suggested by van Creveld,[26] there is insufficient evidence to support this theory. There is similarly no evidence to support the idea of a congenital disturbance in the intercellular ground substance of the media or of other congenital anomalies of the vessels. While there is no other evidence of hypophyseal dysfunction, it remains possible that this condition may be related to progeria. What relation it may have to adult arteriosclerosis is a question for further study.

While it is beyond the scope of this case report to enter into a complete discussion of differential diagnosis, a few salient features of this disease as compared with other diseases from which it must be differentiated are mentioned. These diseases are anomalous origin of the left coronary artery, transposition of the great vessels, idiopathic myocardial degeneration and fibrosis, and glycogen-storage disease of the heart. With regard to anomalous origin of the left coronary artery, inverted T waves are present, usually accompanied with low-voltage waves. $ST_1$ and $ST_2$ may be depressed, and there is no axis deviation, which in infants of 3

months or less may be considered the equivalent of left axis deviation.[3] Roentgen examination may show, in addition to cardiac hypertrophy, a bulge in the left ventricle which is an aneurysmal dilation of the left ventricular wall, the result of complete replacement by fibrous tissue.[4] These findings differed from those of this reported case of arteriosclerosis in that the electrocardiogram of our patient showed right axis deviation with prominent Q waves and "cove-shaped" ST segment in lead I. In addition, the chest roentgenogram (Fig. 2) revealed no evidence of aneurysmal dilatation of the left ventricular wall. In a review of the literature with a report of an additional case, di Sant'Agnese and co-workers state that with glycogen-storage disease of the heart marked left axis deviation occurred in one case and no axis deviation in two others. T waves were inverted in two of three leads in two cases and in three of four leads in one case. The ST segment was depressed in two cases. Low-voltage waves were not present. Chemical demonstration of excessive deposition of glycogen in the biopsy of skeletal muscle and a fairly characteristic type of degeneration of the striated muscle fibers will aid in differentiating glycogen-storage disease of the heart. The electrocardiogram in transposition of the great vessels may show no characteristic abnormalities. However, roentgen examination and angiocardiograms will assist in visualizing the abnormal circulation. Concerning endocardial fibrosis, although the electrocardiogram may show no characteristic abnormalities, eyeground examination may aid in differentiating arteriosclerosis from endocardial fibrosis. In the former condition there are often constriction of arterioles and small hemorrhagic areas.[5]

SUMMARY

A fatal case of medial calcification with internal proliferation of the arteries in a 5-month-old white boy who died of congestive heart failure following myocardial infarction is reported with pathological findings.

There is a brief discussion of several cardiac diseases of infancy which should be differentiated from arteriosclerosis.

Jewish Hospital, York and Tabor Rds. (41).

3. di Sant'Agnese, P. A.; Andersen, D. H., and Mason, H. H.: Glycogen Storage Disease of the Heart, Pediatrics **6**:607-624 1950.

4. Gasul, B. M., and Loeffler, F.: Cardiac Enlargement in Infants, Simulating Coronary Disease, Am. J. Dis. Child. **73**:122-124 (Jan.) 1947.

5. Mitchell, A. G., and Nelson, W. E.: Mitchell-Nelson's Textbook of Pediatrics, edited by W. E. Nelson, ed. 5, Philadelphia, W. B. Saunders Company, 1950, p. 1040.

# Case Reports

## SALMONELLA MENINGITIS

### Recovery from Meningitis Due to Salmonella Sp. (Type Montevideo), with Consideration of the Problem of Salmonella Meningitis

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HENDERSON described in 1948 [1] the occurrence of Salmonella meningitis in three infants and in an excellent review of the literature was able to collect 144 instances of this type of infection in human subjects. Stimulus to further study of the problem was provided by the discovery for the first time of Salmonella meningitis of the Montevideo type. Recovery, which occurred in the infant described, is rare in Salmonella meningitis.

REPORT OF A CASE

L. P., a 7-week-old white boy, was admitted to the Children's Hospital of the University of Texas Medical Branch on Nov. 11, 1949, because of fever, vomiting, and convulsions. When the child was about 3 weeks of age, he was unable to retain his feedings, and it was noted that his temperature was 102 to 103 F. Changes in his feeding routine were made, and injections of penicillin were given, but these measures did not alter his symptoms. During the fifth and sixth weeks of life, temperature elevations persisted and a few convulsions occurred. Five days prior to admission the convulsive seizures became quite severe and were characterized by opisthotonos associated with cyanosis. Two days later a spinal fluid examination was attempted, but blood was said to have been obtained; however, the exact findings are not known. Upon eliciting the past history, it was learned that the patient had been delivered by Caesarean section two weeks prior to the expected date of confinement, and, according to the mother, the section was performed at her request. No resuscitation was required at birth, and the neonatal period was essentially uneventful. The mother believed the infant had been developing normally, judging from her experience with an older sibling. There had been no diarrhea or respiratory tract disease in other persons of the household.

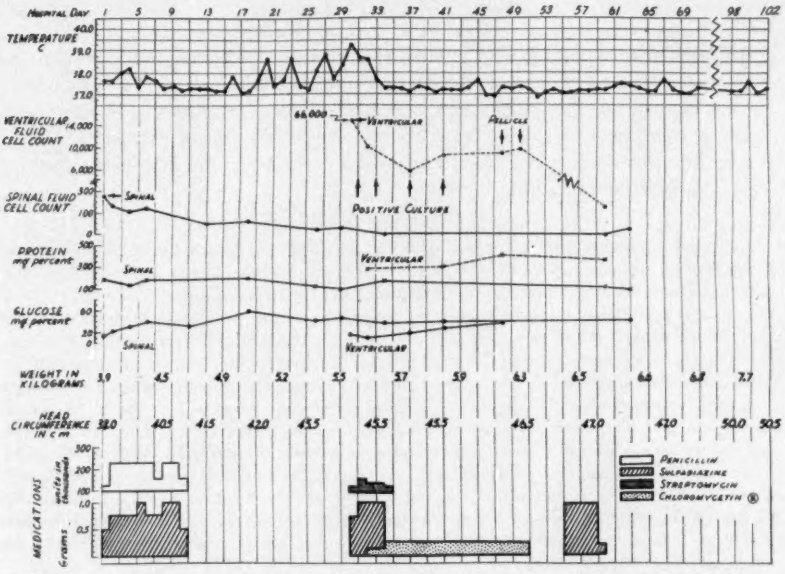
Physical examination revealed an acutely ill-appearing infant who, in spite of a long illness, was well nourished and well hydrated. The weight was 4,040 gm.; the temperature, 37.0 C. (98.6 F.); the pulse rate, 126; the respiratory rate, 36; length, 54.5 cm.; head circumference, 38 cm., and chest circumference 34.5 cm. The anterior fontanel measured 4 by 7 cm., and there was slight separation of the sagittal sutures but no bulging, and the posterior fontanel was almost closed. There was no evidence of otitis media. The pupils were regular and equal and reacted to light. There was an internal squint bilaterally. Nuchal rigidity was not present. The lung fields were normal on percussion and auscultation. The heart was not enlarged; the rate and rhythm were normal. There was a soft systolic murmur at the apex. The liver was palpable 3 cm. below the right costal margin, and the spleen edge was barely palpable. The Moro reflex was present and bilaterally symmetrical. There was no evidence of spasticity. The rooting, sucking, and swallowing mechanisms seemed intact.

From the Department of Pediatrics, University of Texas Medical Branch, Galveston, Texas, and the Department of Microbiology, Stritch School of Medicine of Loyola University, Chicago 12.

1. Henderson, L. L.: Salmonella Meningitis: Report of 3 Cases and Review of 144 Cases from the Literature, Am. J. Dis. Child. **75**:351 (March) 1948.

The laboratory studies may be summarized as follows: The hemoglobin concentration was 11 gm. per 100 ml., and red blood cells numbered 3,000,000 and leucocytes 17,500 per cubic millimeter, with 65% neutrophils, 4% stab forms, 37% lymphocytes, and 4% monocytes. Initial spinal fluid examination revealed 255 cells, with 20% polymorphonuclear forms and 80% lymphocytes, 200 mg. of protein and 16 mg. of sugar per 100 ml., with 103 mEq. of chloride per liter; smears and cultures revealed no organisms. The serum calcium was 9.1 mg. per 100 ml., and the phosphorus was not determined because of an inadequate quantity of serum.

*Course of Disease.*—Sulfadiazine and penicillin were administered to the patient, and, as indicated in the Figure, there seemed to be a gradual improvement in the child's condition during the ensuing two weeks. A gradual fall in the spinal fluid cell count and an increase in the sugar occurred. In spite of the apparent improvement, the child's head size seemed to be increasing rather rapidly. In view of this finding a pneumoencephalogram was attempted on Dec. 9, 1949. About 30 ml. of fluid was removed, but the ventricular system could not be visualized. The following day, a needle was inserted into the region of the right lateral ventricle and grossly purulent fluid




Diagrammatic representation of course of disease in case L. P., a 7-week-old infant with Salmonella sp. (Type Montevideo) meningitis.

was obtained. The ventricular fluid cell count was 60,000; the sugar was 18 mg. per 100 ml. Gram-negative bacilli showing no capsules in anti-A or anti-B Hemophilus influenzae serums were seen on direct smear. Cultures revealed the organism to be a Salmonella. This same organism was isolated repeatedly during the next five ventricular-fluid examinations but never from the spinal fluid. Rectal swab cultures at this time yielded Salmonella. Cultures of the organisms isolated from the ventricular fluid and the stool were sent to Dr. P. R. Edwards, of the Communicable Disease Center, Chamblee, Ga., who identified these as Salmonella sp. (Type Montevideo). On the 30th hospital day streptomycin, together with sulfadiazine, was administered until the sensitivities of the organism to various antibiotic agents could be determined. The results of these studies were as follows:

| | Penicillin, Units/Ml. | Streptomycin, γ/Ml. | Aureomycin, γ/Ml. | Chloramphenicol, γ/Ml. |
|---|---|---|---|---|
| Inhibited by | ... | Slightly by 10 | .. | 5 |
| Tolerated | 5.0 | 5 | 5 | 2.5 |

Sulfadiazine in a concentration of 15 mg. per 100 ml. failed to inhibit growth of the organism; hence its use in treatment was discontinued. The streptomycin therapy was also discontinued on the 32d hospital day. In view of the apparent sensitivity of the organism to chloramphenicol (chloromycetin®), this antibiotic agent was administered. The dose used was 65 mg. per kilogram of body weight per day. The response in regard to fever, appetite, and alertness was prompt.

The enlargement of the head became progressively severer, so that by the 78th hospital day, Jan. 28, 1950, the head circumference had increased to 47.5 cm. Satisfactory ventriculograms

*Summary of Types of Salmonella Organisms, with Incidence in Childhood and Adulthood from Consideration of Eighty-One References in Recent Literature*

| Salmonella | | Age of Patient | | |
|---|---|---|---|---|
| Group | Type | Child | Adult | Unstated |
| A | Paratyphi A | ..... | Margreth.[82] Pansini.[83] Pansini.[83] | Gayoso Rojas.[27] Pestana & Rugai.[34] |
| B | Morbificans | Mackerras & Mackerras.[21] | ..... | ..... |
| | Bredeney | Schweig & Cameron.[38] | ..... | Symmers & Wilson.[37] |
| | Derby | ..... | Hermosilla & others.[20] | Rubenstein & others.[31] |
| | Typhimurium | Atkinson & others.[40] Debre & Mozziconacci.[50] Garcia Rodriguez & others.[59] Green.[63] Henderson.[1] Hormaeche & others.[64] Levinson & others.[70] Margreth.[82] O'Callaghan.[82] Ungar.[87] Veslot & others.[93] Vizcarondo & others.[93] | ..... | Roemer & Grün.[81] Rubenstein & others.[31] |
| | Paratyphi B | Butikofer.[28] Caselli & Tsobaldo.[32] Fontan & others.[60] Gauvreau & Morin.[62] Leenhardt & others.[69] Massengale.[87] O'Callaghan.[82] Wieland.[94] | Ferrabouc & others.[61] Rivet & Cautheron.[85] Ungar.[87] | Bahrenburg & Ecker.[24] Ungar.[87] |
| C | Bareilly | Padnos & Goldin.[57] | ..... | ..... |
| | Choleraesuis | Neter.[54] | ..... | ..... |
| | Manhattan | Janney & others.[46] | ..... | ..... |
| | Newport | Henderson.[1] Pearlman & Gordon.[53] | Rodaniche.[83] | ..... |
| | Oranienburg | ..... | ..... | Hajna & Perry.[5] |
| | Paratyphi C | ..... | ..... | Beattie & others.[30] |
| D | Blegdam | Fournier & Tuo.[87] | ..... | ..... |
| | Dublin | Editorial.[47] | ..... | ..... |
| | Eastbourne | Bornstein & Saphra.[26] | ..... | ..... |
| | Enteritidis | Cathala & Straus.[31] Claudius.[33] Editorial.[47] Green.[63] Marquezy & others.[81] Symmers & Wilson.[87] Vaccaro & others.[90] | Lindberg & Bayliss.[69] | Rupert.[83] |
| | Panama | Albert & others.[15] Henderson.[1] High & Spaulding.[65] Leeder.[68] | ..... | ..... |
| | Typhi | Cannata.[31] Facatselli.[35] Gurevitch.[39] Hageman.[45] Kao.[51] Martinez.[78] Stuart.[84] Wieland.[94] | Derot & Maschas.[29] Lantin & Morales.[71] Symmers & Wilson.[87] | Boquien & Grislain.[27] Chien & Chen.[33] High & Spaulding.[65] Ley.[70] Poinso & Guerin.[82] Sen.[86] |
| E | London | Pestana & Rugai.[34] | ..... | ..... |
| G | Havana | Aballí & others.[18] Cardenas Pupo.[31] Sánchez Santiago.[31] | ..... | ..... |
| | Undetermined | Smith & others.[29] | ..... | ..... |

were not obtained. After removal of fluid via the anterior fontanel, it was possible to inject a large amount of air into the right side and a moderate amount into the left. Roentgenograms revealed numerous collections of globules of air, but the exact location was difficult to determine; however, the roentgenologic consultants felt that this probably was within the ventricles. There was a rounded collection of air in the left frontoparietal region, which, it was believed, may have represented the subdural accumulation of fluid. The comparable area on the right side did not appear to be as extensively involved. The members of the neurological service were consulted, but they felt no further procedures were indicated. The child was sent home Feb. 2, 1950, apparently recovered from the infection but evidently set back in regard to his development.

The final diagnoses were (1) meningitis due to Salmonella sp. (Type Montevideo) with recovery; (2) hydrocephalus secondary to meningitis; (3) mental retardation secondary to meningitis.

## COMMENT

Salmonella sp. (Type Montevideo) was first identified in Uruguay in 1936 in an infant with chronic enterocolitis. This organism has world-wide distribution. It has been isolated mostly from human sources, but also from the turkey and the hen. It is rather surprising that this type has not been previously identified in meningitis, inasmuch as it has been described as the causative organism in some 90 references found in the literature. A closely related type, Salmonella sp. (Type Oranienburg), has been reported on two occasions, once by Henderson [1] in a 5-week-old infant, in whom the meningitis was fatal, and the other by Hajna and Perry,[2] who gave no details concerning their case, other than that it occurred in Maryland.

We have summarized in the Table the incidence of the 11 Salmonella types which have been isolated in cases of meningitis described in 80 separate reports [3]

2. Hajna, A. A., and Perry, C. A.: Salmonella Types Isolated in Maryland Between 1936 and 1943, J. Bact. **49**:518, 1945.

3. (*a*) Aballí, A. A.; Falcón, S.; Sala Panisello, F.; Curbelo, A., and Martínez Cruz, J. A.: Salmonelosis del recién nacido, Bol. Soc. cubana pediat. **9**:123, 1937. (*b*) Albert, D. G.; Cravitz, L., and Townsend, E. H., Jr.: Salmonella Meningitis, Proc. Staff Conf., Rochester Gen. Hosp. **2**:123, 1950. (*c*) Atkinson, N.; Woodroofe, G. M., and Macbeth, A. M.: The Occurrence of Salmonella Types in Australia, Australian J. Exper. Biol. & M. Sc. **25**:25, 1947. (*d*) Bahrenburg, J. H., and Ecker, E. E.: Meningitis Due to Organisms Belonging to the Salmonella Group, J. Infect. Dis. **60**:81, 1937. (*e*) Beattie, C. P.; Lawy, H., and Taylor, J.: Meningitis Due to Salmonella Paratyphi C, Month. Bull. Min. Health & Pub. Health Lab. Serv. **5**:184, 1946. (*f*) Boquien, Y., and Grislain, J. P.: Les formes méningees de la fièvre typhoïde, Semaine hôp. Paris **25**:2411, 1949. (*g*) Bornstein, S., and Saphra, I.: The Occurrence of Unusual Salmonella Species, J. Infect. Dis. **71**:55, 1942. (*h*) Butikofer, H. U.: Pyocephalus paratyphosus B, Schweiz. med. Wchnschr. **78**:761, 1948. (*i*) Cannata, R.: Contributo alla casistica della meningite purulenta da bacillo del tifo, Pediatria **48**:59, 1940. (*j*) Cardenas Pupo, M. D.: Intervención di la microglía en la meningoencefalitis por Salmonella, Rev. med. trop. y parasitol. **4**:55, 1938. (*k*) Caselli, E. G., and Teobaldo, C. T.: Meningitis a bacilo paratífico B en un lactante, Arch. argent. pediat. **10**:416, 1939. (*l*) Cathala, J., and Straus, P.: Les méningites à salmonella du nouveau-né, Nourrisson **35**:200, 1947. (*m*) Chien, T., and Chen, T. K.: Nat. M. J. China **30**:111, 1944; cited by Kao, Y. E.: Typhoid Meningitis in Children: Report of a Case, Chinese M. J. **66**:83, 1948. (*n*) Claudius, M.: Ein Fall einer tödlich verlaufenden mit Meningitis komplizierten Infection mit Gaertner's Bacil, Acta med. scandinav. Supp. 26, p. 91, 1928. (*o*) Debre, R., and Mozziconacci, P.: Streptomycin Treatment of Septicaemia and Meningitis Due to Intestinal Organisms in Infants, Brit. M. J. **2**:451, 1949. (*p*) Derot, M., and Maschas, H.: Méningite aiguë à bacille du groupe typhique, Bull. et mém. Soc. méd. hôp. Paris **54**:1678, 1938. (*q*) Dutrey, M., and Velluz, J.: Méningite et névraxite aiguës paratyphoidiques, Soc. méd. mil. franç., Bull. mens. **33**:138, 1939. (*r*) Bacterium Enteritidis Infection in Infants, editorial, Brit. M. J. **1**:180, 1940. (*s*) Facatselli, N.: Les manifestations méningées et les méningites d'origine eberthienne ou para-typhique, Arch. méd. enf. **42**:615, 1939. (*t*) Ferrabouc, L.; Crosnier, A., and Guichené, J.: Début encéphalitique d'une Fièvre paratyphoïde B, bénigne, Bull. et mém. Soc. méd. hôp. Paris **51**:977, 1935. (*u*) Fontan and others: Méningite à bacille paratyphique B chez un nouveau-né d'un mois: Traitement par la streptomycine, J. méd. Bordeaux **126**:236, 1949. (*v*) Fournier, J., and Tuo, M. K.: Sporadic Salmonella Infections in Shanghai During the Summer of 1948, Chinese M. J. **67**:16, 1949. (*w*) Garcia Rodriguez, R.; Scolpini, V., and Prunell, A.: Meningitis por salmonella typhimurium, Arch. pediat. Uruguay **20**:100, 1949. (*x*) Gauvreau, L., and Morin, J.-E.: Purulent Meningitis Due to Bacterium paratyphosum B Type 3a, in a Newborn, Canad. M. A. J. **60**:169, 1949. (*y*)

*(Footnote continued on next page)*

which have appeared since Henderson's summary. Included in the Table are a few older reports of meningitis due to the typhoid bacillus, as these had not been catalogued by Henderson, yet typhoid meningitis should not be overlooked when the meningitis caused by various types of Salmonella is considered. The typhoid bacillus is now recognized as a member of the genus Salmonella, and its relationship to members of that group is well attested to by its clinical behavior, especially when the meninges are involved. Formerly, it was the custom to distinguish clinically between typhoid and Salmonella infections. Hence, Henderson in citing the paper of Symmers and Wilson [3r''] mentioned only the patients who suffered from Salmo-

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Gayoso, Rojas, B.: Meningitis purulenta producida por paratifus A, Día méd. **3**:949, 1931. (*z*) Green, R.: Note on Salmonella Organisms, Food Poisoning Group, in Food Poisoning, Pyrexias of Unknown Origin, Pus Formation in Joints, and Meningitis, Bull. Inst. M. Research, Federated Malay States (1939), 1940, p. 28. (*a'*) Gurevitch, J.: Typhoid Bacilli in Spinal Fluid, Acta med. orient. **4**:314, 1945. (*b'*) Hageman, P. O.: Purulent Typhoid Meningitis with Recovery: Case Report, Am. J. M. Sc. **195**:497, 1938. (*c'*) Hermosilla, F.; Paredes, L., and Rojas, M.: Septicemia a salmonella derby, Rev. méd. Chile **71**:688, 1943. (*d'*) High, R. H., and Spaulding, E. H.: Human Infections with Salmonella Panama, Am. J. Dis. Child. **72**:181 (Aug.) 1946. (*e'*) Hormaeche, E.; Surraco, N. L.; Peluffo, C. A., and Aleppo, P. L.: Nuevos estudios sobre las diarrheas infantiles de origen infeccioso, An. Inst. Hig. Montevideo **1**:33, 1947. (*f'*) Inaba, F.: Ein Fall von eitriger Typhusbazillenmeningitis, Jahrb. Kurashiki-Zentralhosp. **12**:9, 1937. (*g'*) Janney, F. R.; Conway, J. P., and Beck, K. H.: Meningitis Due to Salmonella manhattan, J. Pediat. **30**:459, 1947. (*h'*) Jundell, I.: A Case of Paratyphoid Meningitis, Acta pædiat. **14**:229, 1932. (*i'*) Kao, Y. E.: Typhoid Meningitis in Children: Report of a Case, Chinese M. J. **66**:83, 1948. (*j'*) Kauffmann, F.: Die Salmonellagruppe, Copenhagen, Munksgaard, 1941, p. 308. (*k'*) National Research Council, Committee on Chemotherapeutics and Other Agents: Streptomycin in the Treatment of Infections: A Report of 1,000 Cases, J. A. M. A. **132**:4 (Sept. 7) 1946. (*l'*) Lantin, P. T., and Morales, S. B.: Unusual Types of Typhoid Infection, J. Philippine M. A. **18**:59, 1938. (*m'*) Leeder, F. S.: Personal communication to High and Spaulding.[3d'] (*n'*) Leenhardt, E.; Boucomont, J.; Labraque-Bordenave, and Barnay: Méningite à para-typhique B chez un nourrisson, Arch. Soc. sc. méd. et biol. Montpellier **18**:94, 1937. (*o'*) Levinson, A.; Kadison, E. R., and Diamond, J. H.: Salmonella Typhimurium Meningitis: Report of 2 Cases and Review of Literature, Am. J. Dis. Child. **80**:290 (Aug.) 1950. (*p'*) Ley, A.: Hematoma subdural (paquimeningitis hemorrágica interna de Virchow) en el curso de una fiebre tifoidea, Rev. clín. españ. **7**:195, 1942. (*q'*) Lindberg, R. B., and Bayliss, M.: Salmonella Types of the Pacific Area, J. Infect. Dis. **79**:91, 1946. (*r'*) Mackerras, M. J., and Mackerras, I. M.: Salmonella Infections in Queensland, Australian J. Exper. Biol. & M. Sc. **27**:163, 1949. (*s'*) Margreth, G.: Rare complicanze meningee e endocardiche nel corso del paratifo A, Gazz. osp. **50**:1039, 1929. (*t'*) Marquezy, R. A.; Bach, C., and Bourgin, R.: Méningite à bacilles de Gartner: guérison par l'association streptomycine-sulfamide, Arch. franç. pédiat. **6**:308, 1949. (*u'*) Martinez, P. D.: Tifoidea y meningitis tifica en un lactante, Bol. méd. hosp. inf., México **1**:57, 1944. (*v'*) Massengale, L. R.: Paratyphoid B Meningitis in Infant: Report of a Case, J. M. A. Georgia **35**:345, 1946. (*w'*) Neter, E.: Microbiologic Aspects of Salmonellosis in Children, New York J. Med. **48**:412, 1948. (*x'*) O'Callaghan, W. P.: Salmonella Organisms in Unusual Sites, Irish J. M. Sc., p. 123, April, 1945. (*y'*) Padnos, E., and Goldin, M.: Salmonella Bareilly Meningitis in a Child Successfully Treated with Intravenous Aureomycin, J. Pediat. **38**:85, 1951. (*z'*) Pansini, G.: Un caso di meningite da paratifo A con eccezionale reperto del liquor, Studium **17**:326, 1927; (*a''*) Il liquor nel cosi detto meningismo tifico (valore diagnostico e terapeutico della puntura lombare), Cervello **6**:278, 1927. (*b''*) Pearlman, L. N., and Gordon, A. S. P.: Salmonella Newport Meningitis, Canad. M. A. J. **60**:483, 1949. (*c''*) Peluffo, E., and Castells, C. E.: Las manifestaciones meningoencephalíticas en la fiebre tifoidea de los niños, Arch. pediat. Uruguay **10**:35, 1939. (*d''*) Pestana, B. R., and Rugai, E.: Salmonelas isoladas de líquido céfaloraquidiano, Ann.

*(Footnote continued on next page)*

nella enteritidis meningitis and omitted reporting on a patient with typhoid meningitis. In the Table there are listed 18 papers which refer to typhoid meningitis, five of which were found in recent literature.[4] While both meningitis and encephalitis are recognized among the complications and sequelae of typhoid, meningitis due to the typhoid bacillus without enteric symptoms is also known. Certain reports described cases of typhoid in which the onset was characterized by symptoms of an acute meningitis, and it was not until later that the typical clinical features of the disease developed. The merging of typhoid and Salmonella infections into a single concept is supported by bacteriological evidence, and recognition of this, no doubt, would prove highly instructive in the further study of the nature and management of these infections.

During the past few years five types of Salmonella which previously had not been identified in meningitis have been described. These types are morbificans, Bredeney, Blegdam, Manhattan, and paratyphi C. It may be pointed out that Henderson reported the occurrence of three types which have not been encountered since his review. These types are anatis, Loma Linda, and New Brunswick. Up to the present, then, 23 types of Salmonella have been definitely identified as the etiological organism in meningitis. It has been found that children have been afflicted about four times as frequently as adult subjects. It is of some interest that seven of the types listed in the Table have been encountered so far only in children; these are morbificans, Manhattan, Blegdam, Dublin, Eastbourne, Havana, and Panama.

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paulist. med. e cir. **39**:373, 1940. (*e″*) Pijan, Warner, and Gibson: Fever: Anorexia: Case Reports, Child. Mem. Hosp. Chicago **3**:159, 1944. (*f″*) Poinso, R., and Guerin, J.: L'encéphalite typhoïdique à forme amyotrophique, Marseille-méd. **82**:293, 1945. (*g″*) Rivet, L., and Cautheron, R.: Un cas de méningoparatyphoïde B chez un malade atteinte de neurosyphilis, Bull. et mém. Soc. méd. hôp. Paris **47**:1373, 1931. (*h″*) Rodaniche, A.: Meningitis à Salmonella newport, Arch. Hosp. Santo Tomás (no. 4) **1**:527, 1946. (*i″*) Roemer, G. B., and Grün, L.: Eitrige Leptomeningitis durch B. enteritidis Breslau (Salmonella typhi-murium), Ärztl. Wchnschr. **3**:276, 1948. (*j″*) Rubenstein, A. D.; Feemster, R. F., and Smith, H. M.: Salmonellosis as a Public Health Problem in Wartime, Am. J. Pub. Health **34**:841, 1944. (*k″*) Rupert, H. G.: Purulent Meningitis Due to Gaertner's Bacillus, Nederl. tijdschr. geneesk. **78**:1763, 1934. (*l″*) Sánchez Santiago, B.: Meningitis a Salmonella, Arch. med. inf. **7**:188, 1938. (*m″*) Schachter, M.: Typhoïde gravidique et encéphalopathie infantile avec malformations multiples, Bull. méd. Paris **60**:353, 1946. (*n″*) Schweig, K., and Cameron, P. J.: Salmonella Bredeney Meningitis in a 3 Month Old Infant, Harlem Hosp. Bull. **1**:41, 1948. (*o″*) Sen, S.: Neurological Complications of Typhoid Fever, J. Indian M. A. **15**:364, 1946. (*p″*) Smith, M. H.; Dormont, R. E., and Prather, G. W.: Subdural Effusions Complicating Bacterial Meningitis, Pediatrics **7**:34, 1951. (*q″*) Stuart, W. E.: Typhoid Meningitis, Brit. M. J. **2**:77, 1948. (*r″*) Symmers, W. St. C., and Wilson, W. J.: On 3 Cases of Cerebro-Spinal Meningitis Associated Respectively with Bacillus Anthracis, Bacillus Typhosus, and Bacillus Enteritidis (Gaertner), J. Path. & Bact. **13**:351, 1908. (*s″*) Taunay, A.: Frequência de algunos agentes microbianos das diarreias, em São Paulo, Ann. paulista de med. **27**:428, 1945. (*t″*) Thiodet, J.: Formes extra-intestinales des fièvres typho-paratyphiques, Algérie méd. **43**:15, 1939. (*u″*) Thouret, G.: Un cas d'encéphalite typhoïdique, Homéop. franç. **23**:98, 1947. (*v″*) Ungar, J.: Salmonella Meningitis, Lancet **1**:125, 1942. (*w″*) Vaccaro, H.; Perez, M., and Valenzuela-P., E.: Salmonelosis y shigelosis en Chile, Rev. chilena pediat. **14**:153, 1943. (*x″*) Veslot, J.; Matet, Y., and Browaeys, J.: A propos d'un cas de méningite purulente à bacillus d'aertryck chez le nourrisson, Nourrisson **36**:176, 1948. (*y″*) Vicklicky, J.: Typhoid Leptomeningitis Arising in Region of Choroid Plexus, Časop. lék. česk. **88**:37, 1949. (*z″*) Vizcarondo, E.; Troconis, C. C., and Pons, B., cited in Year Book of Pediatrics, edited by I. A. Abt and A. F. Abt, Chicago, The Year Book Publishers, Inc., 1946, p. 158. (*a‴*) Wieland, E.: Encephalitis nach Typhus und nach Paratyphus B bei zwei Kleinkindern, Monatsschr. Kinderh. **47**:289, 1930.

4. Boquien and Grislain.[3f] Kao.[3l′] Schachter.[3m″] Sen.[3o″] Stuart.[3q″]

The high fatality rate in Salmonella meningitis sharply indicates that further study is needed. In Henderson's series, death resulted in 128 of the 147 patients, a mortality rate of 87.5%. In the reports listed in the present review (Table), there were 72 fatalities among the 87 cases reported, a death rate of 82.7%. There has been no significant reduction in the fatality rate during the present period of increasing use of antibiotics. However, the favorable reports on the use of the newer therapeutic agents make it imperative to continue the study of this phase of the problem. Up to the present various reports indicate that recovery has followed the use of sulfonamides [5] and also streptomycin.[6] Sulfaguanidine in combination with streptomycin was employed with success in treatment of a patient with S. enteritidis [3t'] meningitis. Recently, Padnos and Goldin [3y'] reported the successful use of aureomycin intravenously in Type Bareilly meningitis. Chloramphenicol was used with benefit in an infant with Type Panama [3b] meningitis. The recoveries have not been limited to a particular type, as the following types have been favorably influenced: paratyphi A,[3d''] typhimurium,[3o', z''] paratyphi B,[3t] Bredeney,[3n''] Manhattan,[3g'] Newport,[7] enteritidis,[3l,t'] Panama,[8] and Bareilly.[3y'] Penicillin was not effective in S. typhimurium [1] or S. paratyphi C [3d] meningitis, nor in one of the S. paratyphi B [3h] type.

In order to facilitate effective therapy and thereby prevent the neurologic complication such as developed in our patient with meningitis due to Salmonella sp. (Type Montevideo), early diagnosis of the infection is of paramount importance.

## SUMMARY

The first recorded case of meningitis due to Salmonella sp. (Type Montevideo) is presented.

The recent literature on Salmonella meningitis contains 87 cases, of which 72 were fatal.

From a consideration of 235 patients with meningitis caused by a member of the genus Salmonella, the occurrence is four times as frequent in children as in adult subjects.

Both successes and failures have been reported in the use of sulfonamides and antibiotics in the treatment of Salmonella meningitis.

5. Henderson.[1] High and Spaulding.[3d'] Vizcarondo and others.[3z'']
6. Cathala and Straus.[3l] Pearlman and Gordon.[3b'']
7. Henderson.[1] Pearlman and Gordon.[3b'']
8. Albert and others.[3b] High and Spaulding.[3d']

# NEUROFIBROMATOSIS IN A NEWBORN INFANT

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NEUROFIBROMATOSIS of von Recklinghausen is considered to be infrequent in children. Leader and Grand [1] reviewed a series of reported cases of children and noted that the disease is as frequent in the male as in the female and that it is usually first noticed, if not at birth, between the ages of 2 and 6 yr. In the early stages, in childhood, the cutaneous pigmentation may be the only manifestation of the disorder, and frequently, because there are no associated signs, the diagnosis is not made. Many years ago Weber [2] called attention to cases in which pigmentation of the skin became evident long before the appearance of neurofibromas of the nerve trunks. In view of the rarity of nodular formation (neurofibromas) at birth, the following case is being presented.

## REPORT OF A CASE

G. F. C. (50-14819), Negro girl weighing 2,500 gm., was born on Aug. 6, 1950. The duration of labor was 12 hr. The delivery was normal. The infant breathed and cried spontaneously. Examination revealed a circular crater-like depression measuring about 4 cm. in diameter on the lateral aspect of the right side of the chest. The base of the crater was covered with solid yellow material. The margins of the crater were composed of indurated purplish-brown elevations. There was a deformity of the chest due to the depression. Scattered over the neck, trunk, and extremities, except for the hands and feet, were firm subcutaneous nodules measuring 1 to 3 cm. in diameter. The skin overlying some of these lesions was hyperpigmented (Figs. 1 and 2).

The mother, a primipara, was 28 yr. of age, and this was her only pregnancy. In September, 1949, because of positive serologic reactions, she received a course of antisyphilitic therapy, consisting of 10 injections of penicillin over a seven-day period. In May, 1950, the patient received 6,000,000 units of penicillin, followed by weekly injections of bismuth and oxophenarsine hydrochloride (mapharsen®) until the week of delivery. Physical examination and roentgenograms of the skeleton during the postpartum period revealed no abnormalities. The father was not available for an examination, but the mother stated that he did not have any skin lesions. The remainder of the family history was unobtainable.

*Laboratory Data.*—A hemogram done on the third day of life revealed a hemoglobin concentration of 19.5 gm. per 100 cc. (Sahli), 6,450,000 red blood cells and 12,400 white blood cells per cubic millimeter, with a normal differential count, and 210,000 thrombocytes (platelets) per cubic millimeter. There was no sickling of the red blood cells. Urinalysis revealed no abnormalities. The blood Kolmer test during the first week gave a 2+ reaction. This test was repeated

From the service of Harry J. Cohen, M.D., Pediatric Department of the Harlem Hospital of New York City, Morris Gleich, M.D., Director.

1. Leader, S. D., and Grand, M. J.: Von Recklinghausen's Disease in Children, J. Pediat. **1**:754 (Dec.) 1932.

2. Weber, F. P.: Cutaneous Pigmentation as an Incomplete Form of Recklinghausen's Disease with Remarks on the Classification of Incomplete and Anomalous Forms of Recklinghausen's Disease, Brit. J. Dermat. **21**:49 (Feb.) 1909.

a month later, and the reaction was reported as negative. Dark-field examinations of several of the lesions revealed no spirochetes. Roentgenograms of the skeleton revealed no abnormalities except of the chest, which showed a compression deformity of the right thorax, with shift of the heart and mediastinum to the left. Bony bridging between several ribs was present. A gastrointestinal series showed no lesions.

*Progress.*—On the second day of life biopsy specimens of a lesion of the right upper arm and of the margin of the crater-like lesion of the right side of the chest were taken. The tissue removed was firm and brownish-white. The results of microscopic examination were reported as follows:

"Examination reveals cutaneous and subcutaneous tissue. The superficial epithelial tissue is of average appearance. Immediately beneath the normal cutaneous tissue, however, one sees

Fig. 1.—Photograph showing crater-like lesion of the chest due to coalescence of neurofibromas.

whorl-like arrangements of delicate nerve fibers surrounded by dense, thickened, hyalinized connective-tissue fibers. The latter take on the pink eosin stain. Within the whorls one sees vacuolation of the nerve fibers with nuclear fragmentation" (Fig. 3).

In retrospect, it was believed that the chest lesion was formed by the coalescence of several neurofibromas, with subsequent central necrosis producing the depression.

The general condition of the child remained satisfactory throughout her hospital stay. Neurological and ophthalmoscopic examinations gave normal results. A few new subcutaneous nodules appeared over the trunk; some of the older lesions became larger, and the hue of the overlying skin deepened. There was minimal healing of the chest lesion. Several lesions on the back and neck became superficially ulcerated. Antibiotic therapy was instituted to prevent secondary infection.

At the age of 2½ mo. the infant was released from the hospital against the advice of the physicians.

COMMENT

Neurofibromatosis is characterized by single or multiple tumors arising from the sheaths of nerves. The disorder is now regarded as a generalized disease involving primarily nervous tissue in any part of the body, with secondary changes in other organs. The disease is considered a congenital malformation of unknown pathogenesis.

Preiser and Davenport [3] reported neurofibromatosis in 43.5% of 115 children who had one parent affected. Gardner and Frazier [4] have traced it through five

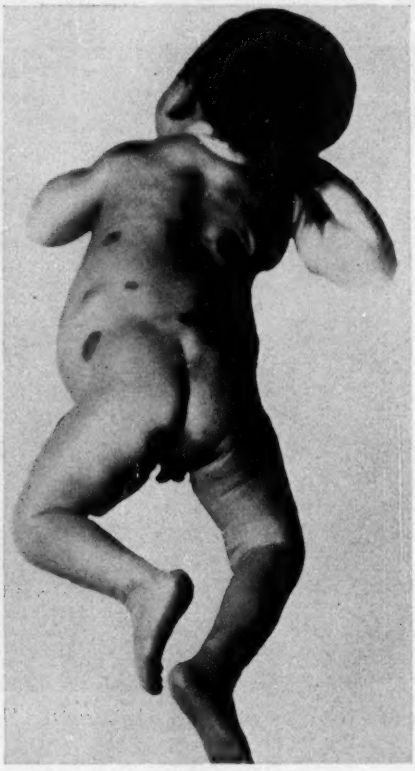

Fig. 2.—Photograph showing scattered pigmented neurofibromas.

generation of affected families and believe that this disease is inherited as a dominant factor. Barber [5] cited a family in which seven of eight surviving children showed

3. Preiser, S. A., and Davenport, C. B.: Multiple Neurofibromatosis (von Recklinghausen's Disease) and Its Inheritance, with Description of a Case, Am. J. M. Sc. **156**:507 (Oct.) 1918.

4. Gardner, W. J., and Frazier, C. H.: Bilateral Acoustic Neurofibromas: Clinical Study and Field Survey of a Family of 5 Generations with Bilateral Deafness in 38 Members, Arch. Neurol. & Psychiat. **23**:266 (Feb.) 1930.

5. Barber, C. G.: Congenital Bowing and Pseudarthrosis of the Lower Leg, Surg., Gynec. & Obst. **69**:618 (Nov.) 1939.

evidence of the disorder, and the mother was literally covered with multiple soft tumors of the skin.

The complete clinical form of von Recklinghausen's disease includes the following manifestations: multiple soft tumors of the skin; nodular formation (neurofibromas) which are usually painless; brownish pigmentation of the skin; bone changes, and

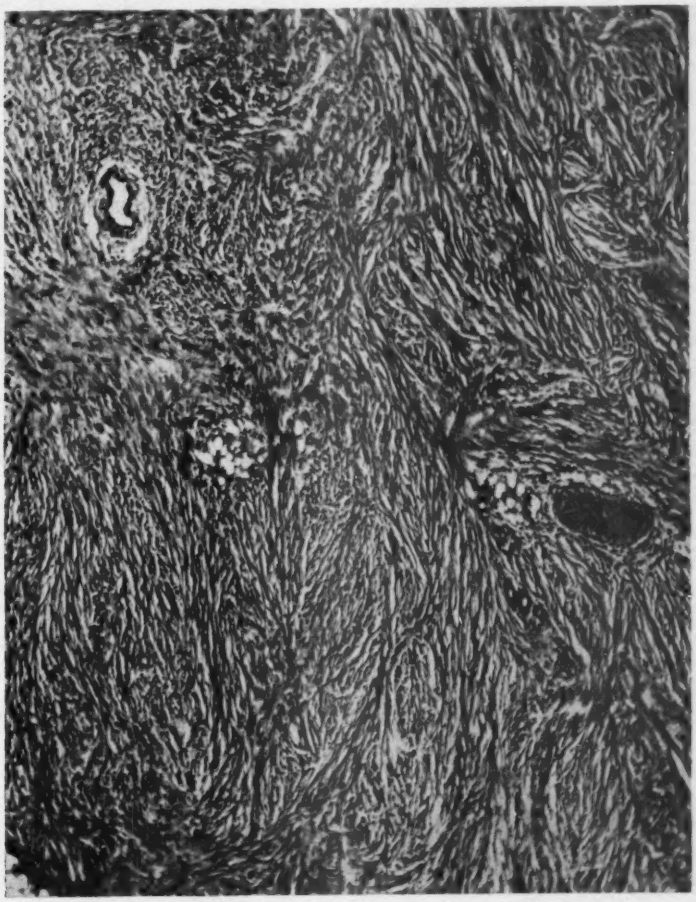

Fig. 3.—Photomicrograph showing the whorl-like arrangements of the nerve fibers. × 100.

mental and physical debility. Every case does not show all the manifestations mentioned. There are incomplete or abortive forms in which only one of the cardinal symptoms is present. Yakovlev and Guthrie [6] have stated that neurofibromatosis may assume a stationary form, a subacute form which is characterized by periods of

6. Yakovlev, P. I., and Guthrie, R. H.: Congenital Ectodermoses (Neurocutaneous Syndromes) in Epileptic Patients, Arch. Neurol. & Psychiat. **26**:1145 (Dec.) 1931.

exacerbation and remission in tumor growth, an acute form showing rapid and generalized development of neurofibromas, or a malignant form undergoing sarcomatous generation and giving rise to metastases. Puberty and pregnancy appear to stimulate the growth of tumors. Stewart [7] emphasized that the diagnosis should be made without removal of a biopsy specimen whenever possible because sarcoma develops frequently after trauma, including operation, especially if removal is incomplete.

Because of the paucity of family history in the case presented, no conclusions can be drawn substantiating the opinion that this is a hereditary disease. Whether or not the infant will present evidence of further involvement is a matter of conjecture.

SUMMARY

A case of neurofibromatosis in a newborn infant is presented. During the patient's hospital stay no involvement other than the cutaneous pigmentation and the subcutaneous nodules was evident.

Solomon Weintraub, Director of Pathology, interpreted the histological sections.

7. Stewart, C. C.: Neurofibromatosis in Children: Report of 2 Cases, New England J. Med. **210**:150 (Jan. 18) 1934.

# ENDOCARDIAL FIBROELASTOSIS

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RECENT pediatric and pathologic literature has reported a larger number of cases of fetal endocardial fibroelastosis than during any previous era.[1] We have studied one of these cases, the features of which were so unique and of such extreme degree that we thought it timely to add our case to the literature. This condition, described in the latter half of the 19th century, is characterized by a non-inflammatory fibrosis of the mural and valvular endocardium, particularly in the left cardiac chambers. Usually both aortic and mitral valves are involved, and often the myocardium is hypertrophied. Occasionally the right side of the heart dilates and hypertrophies, and congenital defects are often found, such as aortic hypoplasia, transposition of the great vessels, patent ductus arteriosus (Botalli), and patent foramen ovale. Although true inflammatory changes are lacking, the condition has been called fetal endocarditis. The endocardium is thickened by an increase in elastic and fibrous tissue. As this process most frequently occurs in the region of the valves and papillary muscles, abnormal thickening, shortening, and nodulation develop at these sites. The clinical entity was first named endocardial fibrosis by Weinberg and Himelfarb in 1943.[2] Prior and Wyatt [1c] in 1950 suggested that the condition should be described as an endocardial dysplasia, which may or may not include the valves, as well as the mural endocardium. The condition may be a developmental error of mesenchymal tissue and perhaps should be placed in the category of a congenital cardiac malformation. Since no person has been described who lived past infancy, probably all patients who have the disease die. The average age at the time of death is 4 to 6 months. Thirty-seven cases have been described to date (June, 1951). Good bibliographies are available in the reports of Collier and Rosahn [1b] and Edmonds and Seelye.[1a]

Clinically, these infants are normal at birth. The onset of signs or symptoms is sudden. Cyanosis is the commonest complaint. Irritability, anorexia, dyspnea, and cough are frequent. Physical examination shows signs of congestive heart failure. The heart may or may not be enlarged, and usually a precordial systolic murmur is heard; occasionally a diastolic one is also present. After the clinical picture develops,

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1. (*a*) Edmonds, H. W., and Seelye, W. B.: Endocardial Sclerosis: Review of Changing Concepts with Report of 6 Cases, Pediatrics **7**:651 (May) 1951. (*b*) Collier, F. C., and Rosahn, P. D.: Endocardial Fibroelastosis, ibid. **7**:175 (Feb.) 1951. (*c*) Prior, J. T., and Wyatt, T. C.: Endocardial Fibro-Elastosis: A Study of 8 Cases, Am. J. Path. **26**:969 (Nov.) 1950.

2. Weinberg, T., and Himelfarb, A. J.: Endocardial Fibroelastosis (So-Called Fetal Endocarditis): Report of 2 Cases Occurring in Siblings, Bull. Johns Hopkins Hosp. **72**:299 (May) 1943.

the duration of life is quite short; usually it is not more than 10 days. Correct diagnosis during life is most exceptional. Left ventricular failure is the usual cause of death. This may be due to stasis within the left ventricular intramyocardial capillaries; degeneration in the papillary muscles is a large factor.

The illnesses often reported in the mother during the pregnancies were rheumatic fever, eclampsia, influenza, syphilis, and nephritis. There is no preponderance of one particular type of illness during the time cardiac formation is taking place. The mothers' illnesses occurred at various stages of pregnancy. Weinberg and Himelfarb [2] were the first to report familial occurrence—two siblings, the second and third pregnancies. These pregnancies were uneventful.

## REPORT OF A CASE

A. P. H. (A-5018), a 2-month-old Negro girl, was admitted to the hospital April 26, 1950, because of "fever, wheezing, racking cough, and weakness" of two weeks' duration. There had been intermittent cyanosis during only the previous two weeks. The formula had been given in inconstant amount, proportion, and composition; no supplementary vitamins were used, and weight gain had been poor or absent. There was no diarrhea, but there were frequent borborygmi and flatulence. Occasional vomiting had been noticed throughout most of her life. The mother's pregnancy was uneventful. The patient was said to have had a normal term delivery. The birth weight was 8 lb. (3,629 gm.) after two hours' labor, with a midwife in attendance. The family history was noncontributory. Five siblings always had good health. The mother had miscarried three times; there were no stillbirths. The mother's Wassermann reaction was negative.

*Results of Physical Examination.*—The temperature was 101.5 F. (38.6 C.); the pulse rate was 180; respirations were 50. The weight was 5 lb. 9 oz. (2,496 gm.). The patient was a weak, cyanotic, malnourished Negro girl, having no apparent respiratory distress. There were moist rales throughout the chest. The heart was enlarged to the left; there were a precordial thrill and a coarse systolic murmur. The abdomen was slightly distended, but the liver was not palpable.

*Results of Laboratory Examination.*—Blood studies showed 16 gm. of hemoglobin per 100 cc. and 6,650,000 red blood cells and 17,250 white blood cells, with a normal differential count, except for 16% nucleated red cells. The tuberculin and Wassermann tests gave negative reactions. Results of urinalysis were normal. The electrocardiogram showed a P-R interval of 10 seconds, with a rate of 150 at an angle of + 115; T waves were upright in all leads; the CR interval in Lead II was abnormal. Myocardial damage was suggested.

*Course in Hospital.*—The immediate treatment given consisted of continuous administration of oxygen, 30,000 units of aqueous penicillin every three hours, and fluids parenterally. Later, incubator care was necessary to maintain normal body temperature. The administration of aureomycin, 50 mg. every four hours, was added on the third hospital day.

Roentgenographic examination of chest on admission was interpreted as showing bronchopneumonia in the upper lobe of the right lung and to less extent in the bases. The large cardiac silhouette "suggested possible congenital heart disease."

On the eighth hospital day cystic lung disease was also suggested by the roentgenogram. On the 22d day bilateral emphysema, with healing fractures of the sixth and seventh ribs on the right, was noticed; artificial respiration given the day before may have caused the fractures. Mediastinal shift was suggested on the 34th day, and by the 41st day the roentgenogram suggested many lung cysts bilaterally, separated by thin fibrous bands.

Normal to subnormal temperature, rapid pulse rate (90 to 120 per minute), and rapid respirations (35 to 50 per minute) prevailed.

Because of extreme respiratory distress a thoracentesis was done on the 49th day, revealing increased intrapleural pressure (forcing out plunger of syringe); a culture of the fluid yielded hemolytic Staphylococcus pyogenes var. aureus. There was only short relief; the patient died five hours later.

*Gross Examination.*—The gross observations were essentially normal except for the heart. The parietal pericardium was smooth and glistening and contained a relatively small amount of

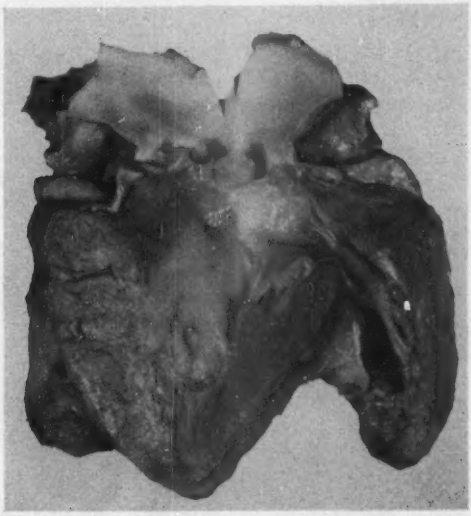

Fig. 1.—Photograph showing markedly thickened intraventricular endocardium and the marked edematous appearance of aortic valves.

Fig. 2.—Thickening of mitral valve and endocardium on left ventricular surface and hypertrophy of left ventricle and of papillary muscles.

fat. The pericardial cavity contained approximately 10 cc. of straw-colored serous fluid but was free from exudate and adhesions. The heart appeared to be enlarged to the left, and the visceral

pericardium showed no gross abnormalities. The heart weighed 32 gm. (normal for this age is 18 to 20 gm.). The heart was diffusely enlarged, but it appeared that the greatest enlarge-

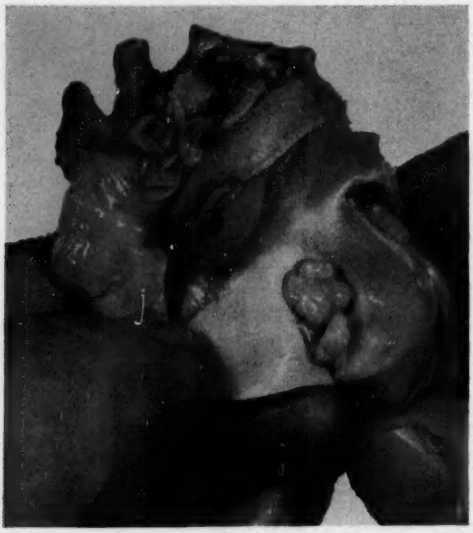

Fig. 3.—Pulmonary valve leaflets, showing extreme thickening and projection above valve-ring base.

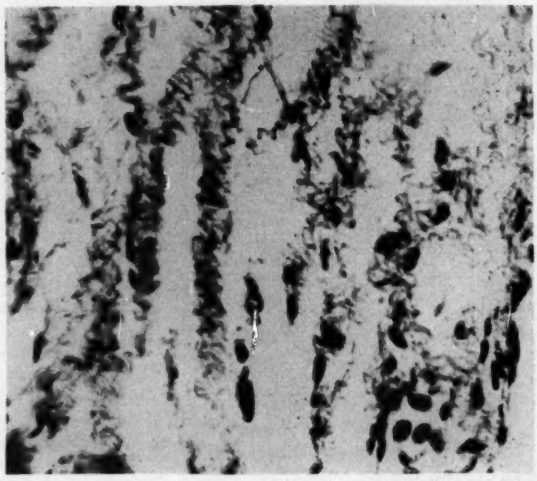

Fig. 4.—Sections of ventricular endocardium. Masson trichrome stain shows wide spaces separating fibrous and connective tissue. These spaces are filled with pale bluish-green material. Marked increase in fibrous connective tissue is readily discernible by increase in green-staining tissue present in endocardium. It is best seen here by large black-staining nuclei. Masson trichrome; × 47.5.

ment was of the left ventricle. The myocardium was a diffuse, pale reddish brown and was firm. The thickness of the left ventricle measured 6 mm. and that of the right ventricle 2 mm. The coronary ostia were patent, and the vessels were smooth and nontortuous. The endocardium on the surfaces of the atrial, ventricular, and the intraventricular septum had a dense grayish-white appearance and was thickened and tough (Fig. 1). The pulmonary, aortic, tricuspid, and mitral valves appeared to be stenosed by a process in which the edges of the valves were markedly enlarged, edematous and soft and had a myxomatous appearance (Fig. 2). The valves' edges projected high above the bases of the valve rings (Fig. 3). The endocardium covering the valves had the same gross appearance as the remainder of the endocardium. The chordae tendineae were neither shortened nor thickened, and the papillary muscles were hypertrophied. There were no other anomalies of the heart or greater vessels.

*Microscopic Examination.*—Lungs: The lungs showed a moderate degree of primary atelectasis.

Heart: The pericardium contained a small amount of fat. The myocardial fibers and bundles were moderately separated by small amounts of edema. The myocardial fibers were hypertrophied, as evidenced by the variation in size and shape of the hyperchromatic nuclei. The endocardium was markedly thickened by interlacing bundles of fibrous connective tissue and elastic fibers. This tissue showed marked edema. The valves were tremendously thickened by a pale, pink-staining, amorphous fibrinoid material. This material was found in the connective tissue spaces of the valve; it had a ground-glass appearance. Special stains, as outlined by Altshuler and Angevine[3] for fibrinoid degeneration, showed in all sections studied changes similar to those described in other conditions as being characteristic of fibrinoid degeneration.[3]

## COMMENT

In this case we were much impressed by the degenerative changes in the endocardium and valves. This change appears to be a widespread form of fibrinoid degeneration similar to that commonly described in the group of collagen diseases.[3] The process of fibroelastic endocarditis has never been placed in this category; we wondered if it is one of the collagenous diseases. With this in mind we studied the alteration with a variety of stains; these included Masson trichrome stain, which yielded a bluish-green appearance with red nuclei (Fig. 4); mucicarmine, which stained red-pink (Fig. 5); toluidine blue rendered a metachromatic appearance (Fig. 6); crystal violet stained dark purple (Fig. 7); phosphotungstic acid-hematoxylin stained very pale yellow-orange (Fig. 8); van Gieson's stain stained the tissues orange-red.

The changes shown by the stains were essentially those described by workers as being characteristic of the collagen diseases.[4] These consist of precipitation of the acid mucopolysaccharide of the ground substance of the connective tissue, the mucinous and homogeneous nature of the ground substance, and the proliferation of the connective tissue with a minimal or moderate inflammatory cell reaction. Do these criteria fit fibroelastic endocarditis? They do in this particular case and probably do in many of the other reported cases.

The etiological basis of the collagen disease is actually unknown, but hypersensitivity has been suggested. In our own case, as in others reported, there is no known etiological agent. Infection has been reported in some of the mothers during pregnancy.

3. Altshuler, C. H., and Angevine, D. M.: Histochemical Studies on the Pathogenesis of Fibrinoid, Am. J. Path. **25**:1061 (Sept.) 1949.

4. Klemperer, P.: The Concept of Collagen Diseases, Am. J. Path. **26**:505 (July) 1950.

It is well known that there is a predilection in the collagenous group of disease for endothelium-lined surfaces and endocardial changes. The termination is almost universally fatal in the collagenous group of diseases. Our patient lived two months; the average survival is to about 6 months of age; the oldest patient of whom we were able to find a description was 5 years of age.

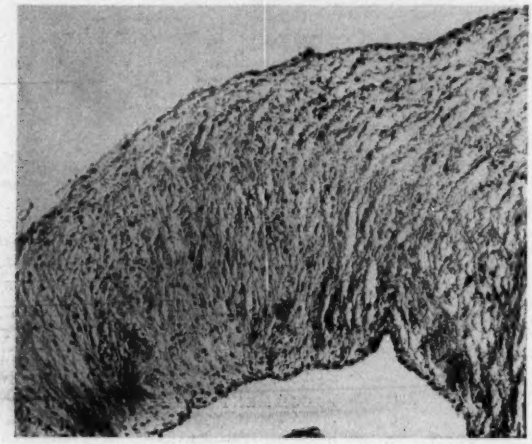

Fig. 5.—Section of mitral valve. The many small spaces are filled with red-pink-staining material. It is also apparent that there is an increase in fibroelastic tissue. Mucicarmine; × 10.

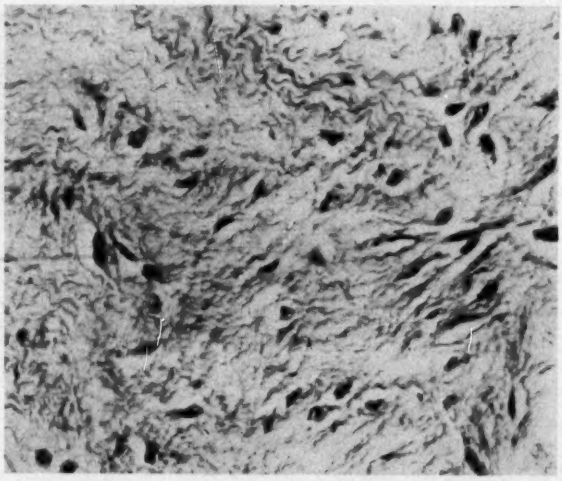

Fig. 6.—Section of left ventricular endocardium. Muddy appearance represents fibrinoid degeneration between fibrous and elastic tissue bundle. Toluidine blue; × 47.5.

On the above evidence, we believe that the case of endocardial fibroelastosis that we have examined, and probably others, fits the criteria for the collagenous diseases and properly should be placed in this group.

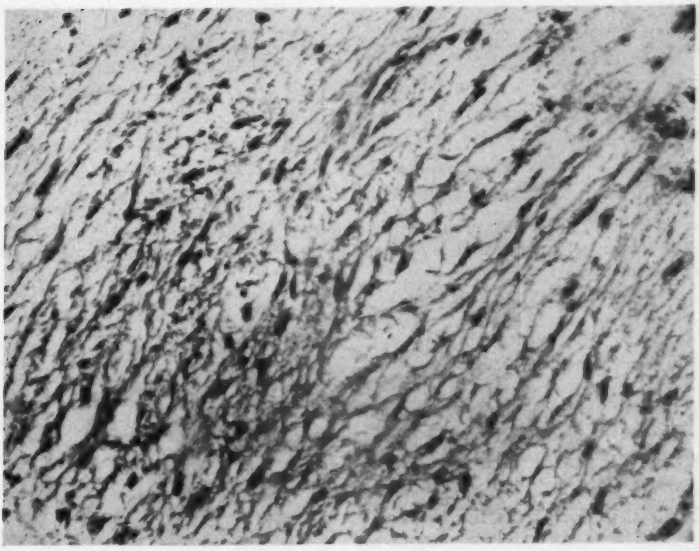

Fig. 7.—Section showing marked widening of fibrous connective tissue spaces by fibrinoid degeneration and increase of collagenous tissue. Crystal violet; × 47.5.

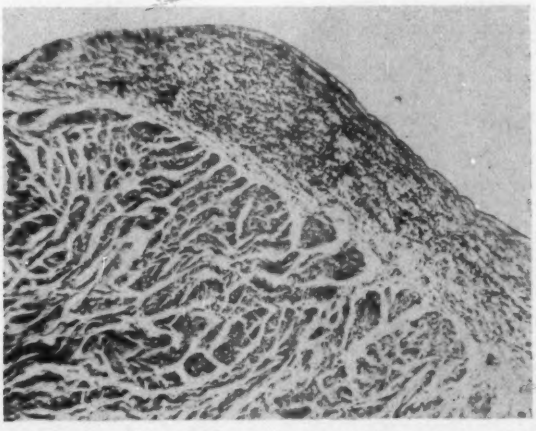

Fig. 8.—Section showing thickened endocardium in relation to hypertrophied myocardium. Phosphotungstic acid-hematoxylin; × 10.

SUMMARY

With this report we add another case of fetal fibroelastosis to the literature. It was unique in the extensive involvement of all cardiac valves and the endocardium of all chambers. There was left ventricular hypertrophy.

After an extensive study of the microscopic changes, we believe it is proper to call this entity one of fetal endocardial fibroelastosis. We were impressed by the close resemblance of this condition to that group of diseases known as collagen diseases. Many special stains on sections from the heart valves showing fibrinoid degeneration, as outlined by Altshuler and Angevine, in this particular case strongly suggested that this disease should belong to the collagen disease group.

Dr. A. Nettleship, Professor and Head, Pathology Department, University of Arkansas School of Medicine, first suggested to us that fetal fibroelastosis is probably a collagen disease (private communication).

Photographs were made by Greer H. Lile.

# ADENOMA OF BRONCHUS IN A NINE-YEAR-OLD CHILD

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AND
AUBRE DE L. MAYNARD, M.D.
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ADENOMA of the bronchus is a rare tumor in the pediatric age group. It is probably one of the most controversial neoplasms in thoracic surgery because of its malignant tendencies. Since the inception of the Children's Tumor Registry about 10 years ago, no cases have been reported directly to the Registry.[1] However, several large series of cases of bronchial adenoma which include those of a few children 11 yr. of age or older have been reported in the literature.[2]

The following case of bronchial adenoma is being presented not only because of the condition's rarity but also because of the development of the middle-lobe syndrome as a complication.

## REPORT OF A CASE

*First Admission.*—A. T. (49-12860), a 9-yr.-old Negro girl, was admitted to Harlem Hospital on Aug. 24, 1948, with a history of a chronic, nonproductive cough of four months' duration and hemoptysis (approximately 240 cc. of bright red blood) the day prior to admission.

The past medical history was noncontributory, and the family history was significant only in that both parents had received antisyphilitic treatment in 1942 and the paternal grandmother had died as a result of a gastric neoplasm.

On physical examination, the temperature was 101.3 F. (38.5 C.); the pulse rate was 84 per minute, and the respiratory rate was 20 per minute. The patient weighed 28.6 kg.

The pertinent physical findings were confined to the right side of the chest, where there were slight dulness on percussion posteriorly at the base and an occasional crepitant rale on auscultation in this region.

The important laboratory data were as follows: The Mantoux reaction with 1 mg. of old tuberculin was positive; the erythrocyte count was 3,920,000 per cubic millimeter, with a hemoglobin concentration of 10 gm. per 100 cc. (Sahli); the leucocyte count was 13,100 per cubic millimeter, with 71% polymorphonuclear forms, 7% transitional forms, 21% lymphocytes, and 1% eosinophils; the blood Kahn reaction was positive on two successive tests; the cerebrospinal fluid, the erythrocyte-sedimentation rate, and the urine on analysis were normal; sputum studies and repeated gastric washings were negative for acid-fast organisms.

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From the Pediatric and Surgical Services of Harlem Hospital, Morris Gleich, M.D., Pediatric Director, and Louis T. Wright, M.D., Surgical Director.

1. Stewart, F. W.: Personal communication to the author.

2. (*a*) Rosenblum, P., and Klein, R. I.: Adenomatous Polyp of the Right Main Stem Bronchus Producing Atelectasis, J. Pediat. **7**:791, 1935. (*b*) Wessler, H., and Rabin, C. B.: Benign Tumors of the Bronchus, Am. J. M. Sc. **183**:164, 1932. (*c*) Goldman, A., and Stephens, H. B.: Polypoid Bronchial Tumors with Special Reference to the Bronchial Adenomas, J. Thoracic Surg. **10**:327, 1941. (*d*) Jackson, C. L.; Konzelman, F. W., and Norris, C. M.: Bronchial Adenoma, ibid. **14**:98, 1945. (*e*) Moersch, H. J.; Tinney, W. S., and McDonald, J. R.: Adenoma of the Bronchus, Surg., Gynec. & Obst. **81**:551, 1945. (*f*) Souders, C. R., and Kingsley, J. W., Jr.: Bronchial Adenoma, New England J. Med. **239**:459, 1948. (*g*) Som, M. L.: Adenoma of the Bronchus: Endoscopic Treatment in Selected Cases, J. Thoracic Surg. **18**:462, 1949. (*h*) Naclerio, E. A., and Langer, L.: Adenoma of the Bronchus—Review of 15 Cases, Am. J. Surg. **75**:532, 1948.

A roentgenogram taken on admission (Fig. 1) revealed an area of increased density of the greater part of the middle lobe of the right lung. The patient remained afebrile and comfortable; however, the clinical and roentgenographic findings persisted.

Bronchoscopy on Sept. 29 revealed the carina in the midline, but the procedure had to be discontinued because of profuse hemorrhage.

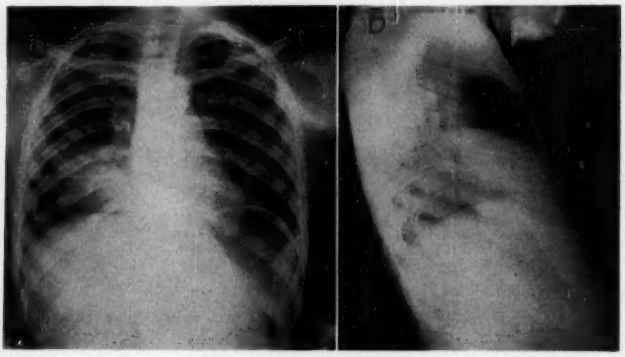

Fig. 1.—Area of increased density in greater part of middle lobe of right lung present on first admission, Aug. 24, 1948.

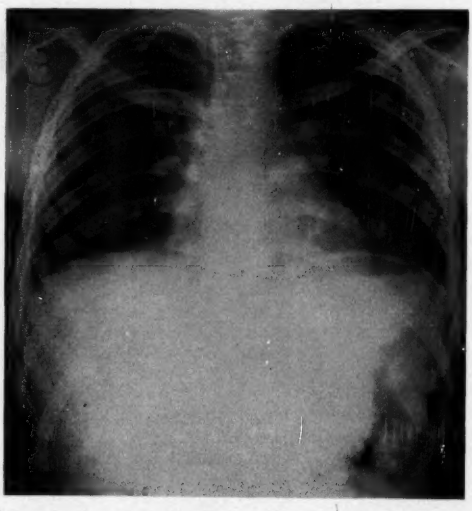

Fig. 2.—Post-biopsy clearing of the density in middle lobe of right lung on Oct. 20, 1948.

Bronchoscopy was repeated on Oct. 18. A fleshy, polypoid, red smooth mass was visualized arising from the anteromesial wall of the right main-stem bronchus at the level of the middle-lobe spur protruding into the middle-lobe bronchus. A biopsy specimen was taken, which was reported as chronic inflammatory tissue.

A roentgenogram taken two days after the biopsy revealed a clearing of the previously described density in the middle lobe of the right lung (Fig. 2).

Further therapy was refused by the parents, and the child was released from the hospital against advice.

*Second Admission.*—The patient was readmitted to the hospital on July 14, 1949. Since leaving the hospital eight months previously, she continued to have a chronic, nonproductive cough. Eleven days prior to admission, the patient had an episode of hemoptysis, and she continued to have daily bouts thereafter. The patient was seen in the clinic, and hospitalization was advised. Active antisyphilitic therapy had been instituted for congenital syphilis shortly after the first admission.

On physical examination, the temperature was 100.4 F. (38 C.); the pulse rate was 102 per minute, and the respiratory rate was 48 per minute. The weight was 33.6 kg.

Again, the pertinent physical findings were limited to the right side of the chest. There was dulness anteriorly and posteriorly from the fourth rib down, with decreased breath sounds over this area.

A roentgenogram taken on July 14 revealed a recurrence of the area of increased density in the mesial portion of the right middle lobe (Fig. 3).

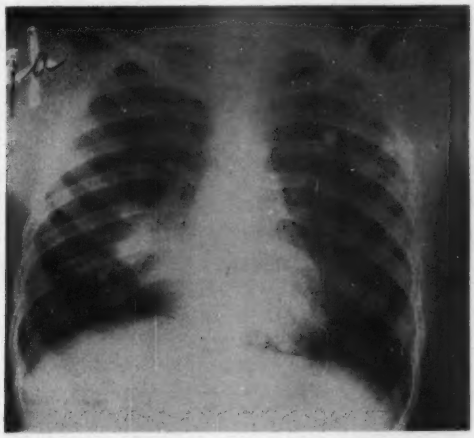

Fig. 3.—Recurrence of density in middle lobe of right lung on second admission, July 14, 1949.

The patient had several episodes of hemoptysis while in the ward. Since the parents objected to a thoracotomy, bronchoscopic removal of the polypoid mass with biopsy forceps was done. The specimen, histologically, was an adenoma of the bronchus (Fig. 4).

A roentgenogram was taken one week after the removal of the mass. It was interpreted as showing some clearing of the density in the middle lobe of the right lung. The patient was discharged to the clinic for follow-up care.

*Third Admission.*—One year and four months after the first admission, the patient re-entered the hospital, on Dec. 17, 1949, for definitive surgical treatment. Since leaving the hospital three months previously, she continued to expectorate blood daily and to complain of lassitude, anorexia, and occasional dyspnea.

The roentgenologic findings were the same as on the previous admissions (Figs. 1 and 3).

The operation was performed on Dec. 27. With the child under endotracheal ether anesthesia, the right pleural cavity was entered. In view of the atelectasis of the right middle lobe with binding adhesions to the lower lobe, the pericardium, and the posterior parietal pleura, pneumonectomy and right phrenicectomy were performed.

Pathologically, the right middle lobe was firm and noncrepitant; the bronchus and bronchioles leading to the middle lobe showed markedly injected mucosa with some grayish-blue mucoid material; the bronchus to the middle lobe was slightly compressed, and there were

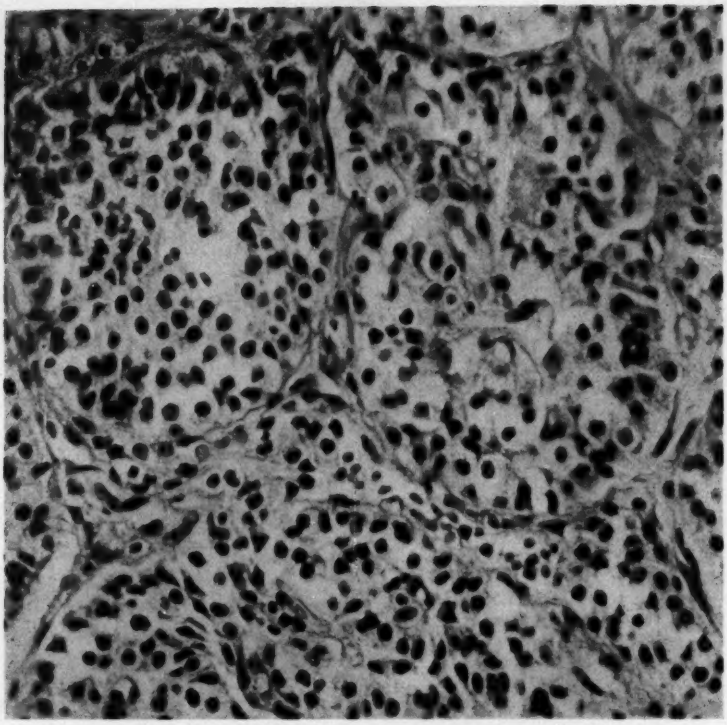

Fig. 4.—Photomicrograph of bronchial adenoma removed by biopsy forceps in August, 1949. × 500.

Fig. 5.—Roentgenogram taken 10 mo. after the pneumonectomy and thoracoplasty, on Oct. 17, 1950.

enlarged peribronchial lymph nodes. No polypoid mass was seen. The portions of both the upper and the lower lobes in contact with the middle lobe were indurated and atelectatic.

Microscopically, there were scattered areas of atelectasis, pneumonitis, bronchiectasis, and fibrosis. There was an area in the bronchus to the right middle lobe that showed hemorrhage and granulation tissue which was thought to be the site of the adenoma, but no adenomatous tissue was present.

Underwater chest drainage and intramuscular and aerosol administration of penicillin were instituted. Fluids intravenously, blood transfusions, and general supportive therapy were given.

Five weeks after the pneumonectomy, on Feb. 9, 1950, a thoracoplasty was performed on the right side, with the removal of the second through the fifth ribs, inclusive.

The postoperative course was uneventful. The patient was comfortable and active in the ward. She was discharged to a convalescent home for follow-up care.

The patient was seen on Oct. 17, 1950. Her general condition was excellent, and she was free of any symptoms. A roentgenogram taken at this time revealed a homogeneous density in the right hemithorax, with evidence of a thoracoplasty. Despite the thoracoplasty there was displacement of the mediastinum and trachea to the right (Fig. 5).

## COMMENT

The symptoms and the clinical course of the bronchial adenoma depend upon the location of the tumor, its vascularity, and its slow growth.[2c]

If the adenoma encroaches upon the lumen of a large bronchus, as it did in this case, the symptoms of bronchial obstruction are produced. Initially, there may be dyspnea, wheezing, nonproductive coughing, fleeting chest pain, and postural respiratory discomfort. Secondarily, the continued obstruction may produce pulmonary suppuration, with symptoms of recurring pneumonia, bronchiectasis, abscess, and empyema.

The slow growth of the adenoma may permit the development of chronic suppuration and secondary toxemia, such as lassitude, a low-grade fever, productive cough, anemia, anorexia, dyspnea, and pleuritis pain.

The foremost symptom of bronchial adenoma is hemoptysis, which is attributable to the marked vascularity of this tumor. Pulmonary hemorrhage may also be associated with the secondary suppuration, as occurred in our case.

Pathologically, the adenoma has three morphological types. The first is pedunculated and entirely endobronchial; the second has a broader attachment and contains a large intramural portion, and the third is composed of an endobronchial and extrabronchial portion.[3]

Grossly, *in situ*, as seen through the bronchoscope, the tumor is freely movable, polypoidal, soft, and smooth, and pink, gray-red, or purple. It is covered by bronchial mucosa and may be crossed by blood vessels.

Microscopically, the bronchial adenoma is composed of small, round, regular cells which attempt to group themselves into patterns, e. g., alveolar, columnar, nodular, or mosaic.[2b]

The importance of early recognition and the removal of a bronchial adenoma cannot be overemphasized in view of the changed opinion regarding its benignity. Anderson in 1942 reported a case of an adenoma with metastases to the liver.[4]

3. Bruns, H., and Goldman, A.: The Differentiation of Benign from Malignant Polypoid Bronchial Tumors, Surg., Gynec. & Obst. **71**:703, 1940.

4. Anderson, W. W.: Bronchial Adenoma with Metastases to the Liver, J. Thoracic Surg. **12**:351, 1942.

Goldman in 1949 presented a report on five patients showing malignant qualities in bronchial adenomas.[5] Surgical specimens often reveal invasion of the adjacent tissue, infiltration of the bronchial wall, and metastases in the tracheobronchial lymph nodes.[6]

Bronchoscopic biopsy specimens may be misleading and inconclusive, as in this case on the first admission. The characteristic patterns are often not obtained because the biopsy forceps may not penetrate deeply enough into the tumor.

There are two generally accepted approaches to the treatment of adenomas of the bronchus:

The first type of treatment is bronchoscopy, with the implantation of radon seeds, electrocoagulation, forceps removal, or a combination of these procedures as recommended by the more conservative groups.[2d]

The second type of treatment is surgical extirpation by either lobectomy or pneumonectomy. This has become the preferred method of treatment because of the possibility of the adenoma being malignant.[6]

The patient here reported on was initially treated conservatively because the parents objected to a thoracotomy, but the development of the middle-lobe syndrome left no doubt that the more definitive surgical treatment should be instituted.

The middle-lobe syndrome was described by Graham and his associates in 1948. They felt that middle-lobe atelectasis with secondary suppuration was due to bronchocompression from the bronchial lymph nodes with bronchostenosis.[7] Actually, the syndrome may occur in any lobe or either lung, but the right middle lobe is most susceptible because of its poor drainage.[8]

It is our belief that this is the youngest patient with proved bronchial adenoma described. The adenoma was of the pure endobronchial type, and it was completely removed bronchoscopically. However, the bronchostenosis and the bronchocompression produced by the adenoma and the adjacent enlarged peribronchial lymph nodes resulted in irreversible chronic suppurative disease of the lung. This complication, in addition to the possibility of a malignant growth, necessitated surgical intervention.

SUMMARY

The case of a 9-yr.-old child with an adenoma of the right-middle-lobe bronchus is presented. The patient was treated conservatively with bronchoscopic removal of the tumor. The development of chronic irreversible changes in a middle-lobe syndrome necessitated surgical intervention.

Dr. Solomon Weintraub, Director of Laboratories, made the pathological interpretations and permitted use of the specimen.

5. Goldman, A.: The Malignant Nature of Bronchial Adenoma, J. Thoracic Surg. **18**:137, 1949.

6. Naclerio and Langer.[2h] Discussion on Goldman [5] and Rabin, C. B., and Neuhof, H.: Adenoma of the Bronchus, J. Thoracic Surg. **18**:155, 1949.

7. Graham, E. A.; Burford, T. H., and Mayer, J. H.: Middle Lobe Syndrome, Postgrad. Med. **4**:29, 1948.

8. Paulson, D. L., and Shaw, R. R.: Chronic Atelectasis and Pneumonitis of the Middle Lobe, J. Thoracic Surg. **18**:747, 1949.

# Progress in Pediatrics

## CAUSES OF CONGENITAL DEFECTS

A Review

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AND
T. D. FAINSTAT, M.Sc.
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### THEORIES OF CAUSATION OF CONGENITAL DEFECTS IN HUMAN BEINGS

WHAT CAUSES congenital defects? Interest in this problem increases as the control of bacteriological and nutritional sources of ill-health continues to improve and as the congenitally defective group makes a proportionately greater contribution to the infant mortality and morbidity rates.[1] Yet there is probably no pediatric field in which more widely divergent views are held. This paper will discuss some of these opinions and review briefly the rapidly growing body of literature on experimentally produced congenital defects in mammals.

1. *Defects with Genetic Causation.*—"Hereditary" defects are defined as "those determined by factors transmitted through the germ cells," while "congenital" defects are defined as "those present at birth." Obviously, congenital defects are not necessarily hereditary, and hereditary abnormalities are not necessarily congenital. The terms "hereditary" and "genetic" are used synonymously.

It is well established that in some families some congenital defects follow a simple Mendelian pattern of transmission, showing that they can be produced by changes at a single gene locus. These include hydrocephalus,[2] cataract,[3] cleft palate,[4] cleidocranial dysostosis,[5] various deformities of the extremities, such as claw hand,[6] split foot, polydactylism and brachydactylism,[7] chondrodystrophy,[8] dislocation of the hip,[9] and many others.[10] Such cases, plus the data indicating that when both members of a set of twins have a congenital defect the twins are usually monozygotic (i. e., genetically identical), led Macklin[11] to the rather overenthusiastic conclusion that "inherent defects in the determiners for development are responsible for the vast majority of congenital malformations in man."

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From the Department of Genetics, McGill University (Dr. Fraser and Mr. Fainstat) and the Children's Memorial Hospital (Dr. Fraser).

1. Miller, H. C.: Pediatrics **5**:320, 1950.
2. Bickers, D. S., and Adams, R. D.: Brain **72**:246, 1949.
3. Saebø, J.: Brit. J. Ophth. **33**:601, 1949.
4. Straith, C. L., and Patton, H. S.: Bilateral Congenital Mucous Cysts in 3 Generations, J. A. M. A. **123**:693 (Nov. 13) 1943. Test, A. R., and Falls, H. F.: J. Oral Surg. **5**:292, 1947.
5. Soule, A. B., Jr.: J. Bone & Joint Surg. **28**:81, 1946.
6. Stiles, K. A., and Pickard, I. S.: J. Hered. **34**:341, 1943.
7. Lewis, T.: Treasury Hum. Inher. **1**:6, 1909.
8. Böök, J. A.: Hereditas **36**:161, 1950.
9. Corrigan, C., and Segal, S.: Canad. M. A. J. **62**:535, 1950.
10. Kemp, T.: Heredity **1**:259, 1947.
11. Macklin, M. T.: Am. J. Obst. & Gynec. **32**:258, 1936.

Murphy [12] was led to a similar conclusion from a study of the obstetric histories of 501 mothers who had borne children that died in infancy of a congenital defect. He found that 25% of the subsequent pregnancies had an unfavorable outcome, and that almost half of these were live births with a congenital malformation. This is an important finding which should be kept in mind when advising parents of a child with a lethal defect about the prognosis for future pregnancies. It is desirable, however, to have estimates of the risk of unfavorable outcome for each type of defect separately, since this risk varies from type to type. No relationship could be demonstrated between the occurrence of malformations and various environmental factors, including occupation of the father, chronic disease in the mother, use of contraceptives, month of conception, legitimacy, and placenta previa. In families with more than one defective child, the same defect recurred in more than half the cases (23 recurrences in 40 families) and there was a positive correlation between incidence of defect and maternal age. However, it is difficult to see how these facts led Murphy to conclude that "gross, human, congenital malformations arise solely from influences which affect the germ cells prior to fertilization." Many of the mothers were anemic, and many were on diets deficient in minerals and vitamins. In the absence of adequate controls the significance of these and other findings cannot be assessed; hence we do not feel that etiological factors extrinsic to the embryo but common to successive pregnancies were ruled out in his study.

Our knowledge of the genetically determined group of congenital defects in human beings is supplemented by studies of a large number of corresponding defects in experimental mammals, some of which have been thoroughly worked out embryologically.[13]

2. *Defects with Environmental Causation.*—A second and still fairly small group of congenital defects can be clearly related to a definite environmental agent,[14] although there is some experimental evidence to suggest that genetic factors may have an influence in these cases as well. The most outstanding of these agents is the rubella virus, which when it infects a pregnant mother in the first trimester may cause one or more of a group of abnormalities, including cataract, heart defects, and deaf-mutism.[15] Several of these defects resemble closely those found in the obviously hereditary group. Each of them has its counterpart in the "sporadic" group with no obvious genetic or environmental cause. Only the characteristic association of several defects in one child and the history of maternal rubella infection lead one to the proper diagnosis. Clinically, one needs to know how great the risk of defect in the child will be when the mother contracts rubella in the first trimester. It is now thought that about 40% or less of the offspring of such preg-

12. Murphy, D. P.: Congenital Malformations, ed. 2, Philadelphia, J. B. Lippincott Company, 1947.

13. Grüneberg, H.: (*a*) Rev. Suisse de Zool. (supp. 1) **57**:129, 1950; (*b*) The Genetics of the Mouse, London, Cambridge University Press, 1943; (*c*) Animal Genetics and Medicine, London, Hamish Hamilton Medical Books, 1947. (*d*) Gruenwald, P.: Mechanisms of Abnormal Development, Arch. Path. **44**:398 (Oct.); 495 (Nov.); 648 (Dec.) 1947. (*e*) Robertson, G. G.: J. Exper. Zool. **89**:197, 1942. (*f*) Gluecksohn-Schoenheimer, S., and Dunn, L. C.: Anat. Rec. **92**:201, 1945. (*g*) Schoenheimer, S.: Growth **9**:163, 1949.

14. Warkany, J.: Am. J. Ment. Deficiency **50**:231, 1945. Warkany, J.; Roth, C. B., and Wilson, J. G.: Pediatrics **3**:462, 1948.

15. Gregg, N. M.: Tr. Ophth. Soc. Australia **3**:35, 1942. Swan, C.; Tostevin, A. L., and Black, G. H. B.: M. J. Australia **2**:889, 1946.

nancies will show defects,[1] although earlier estimates, based on highly selected data, were much higher than this.[16] Ingalls [17] relates the type of defect to the embryological events occurring at the time of infection. Whether other maternal infections can also cause defects in the offspring has not yet been definitely established.[18] (We will not consider here conditions such as syphilis and toxoplasmosis which are considered to cause embryonic disease rather than developmental aberrations.)

Another environmental agent which produces congenital defects is maternal irradiation (x-ray or radium) in therapeutic doses during pregnancy.[19] Here again, the incidence of defects in the offspring of mothers so treated is not accurately known, owing to the difficulties involved in getting a well-controlled and unbiased series of cases.

It cannot be disputed, then, that some congenital malformations are caused by environmental agents, but we do not agree with the categorical, and often-quoted [20] view of Mall [21] that

> . . . it is perfectly clear that monsters are not due to germinal and hereditary causes, but are produced from normal embryos by influences which are to be sought in their environment.

This statement is based on an exhaustive study of 1,000 aborted embryos, of which nearly 40% were pathological to some degree, and, while great credit is due Mall for his admirably thorough morphological observations, his conclusions must be revised in the light of more recent knowledge. For instance, he stated:

> It seems to me that . . . all kinds of anatomical anomalies and variations of the extremities like polydactyly . . . are germinal and cannot be produced experimentally.[22]

We will discuss in a later section the production of just such anomalies by experimental means. Again, Mall declared:

> Other monsters in which more or less of the foetus is destroyed, as in iniencephaly, spina bifida, anencephaly, cyclopia and club-foot . . . are not germinal but are produced in some mechanical way.

The hereditary factors in the etiology of anencephaly and clubfoot will be discussed below. Suitable genetic data on the severer types of developmental defect which may cause the embryo to abort are very difficult to obtain in human beings, although it is interesting to note in this regard the observation of Hertig [23] that of 26 early ova found in histologically normal endometria, 10 were abnormal, owing to causes presumed to be genetic.

To support the idea of genetically controlled disturbances of fundamental embryological processes, there are several well-established examples in mice of single gene changes which when homozygous cause developmental disturbances so

16. Levinson, E. D.: McGill M. J. **18**:183, 1949.

17. Ingalls, T.: New England J. Med. **243**:67, 1950.

18. (*a*) Miller.[1] (*b*) Landtman, B.: Arch. Dis. Childhood **23**:237, 1948. (*c*) Stevenson, S. S.; Worcester, J., and Rice, R. G.: Pediatrics **6**:37 and 208, 1950. (*d*) Warkany, J.: Etiology of Congenital Malformations, in Advances in Pediatrics, New York, Interscience Publishers, Inc., 1947, Vol. 2, p. 1. (*e*) Ingalls, T. H.: Etiology of Mongolism, Am. J. Dis. Child. **74**:147 (Aug.) 1947.

19. Murphy, D. P.: Surg., Gynec. & Obst. **48**:766, 1929.

20. Greenhill, J. P.: Am. J. Obst. & Gynec. **37**:624, 1939.

21. Mall, F. P.: Am. J. Anat. **22**:49, 1917.

22. Mall, F. P.: J. Morphol. **19**:1, 1908.

23. Hertig, A. T., in discussion on Warkany, J.: Obst. & Gynec. Surv. **3**:693, 1948.

severe as to cause death of the affected embryos.[13e-g] The medical significance of such gene-controlled aberrations is emphasized in a stimulating discussion by Grüneberg.[13e]

We agree with Mall that the ova found in most tubal pregnancies are defective probably because of their unsuitable environment, but we do not agree that this argument applies to all pathological ova. An embryo may implant on unhealthy endometrium, fail to develop normally, and then abort, as Mall suggests, or an embryo may develop abnormally owing to causes inherent in itself which eventually cause it to abort. The evidence discussed above indicates that each of these mechanisms produces its share of abortions.

3. *Defects with Obscure Causation.*—The great majority of congenital defects show no clear-cut pattern of inheritance and no definite environmental cause, although they may be clinically indistinguishable from those which have an obvious genetic or environmental origin. Large-scale analyses, particularly by the Scandinavian geneticists, have established that with some types of defect the families of affected patients contain more affected persons than expected if the defect were distributed at random. This applies to such conditions as cleft lip and/or palate,[24] clubfoot,[25] and anencephaly.[26] An increased incidence of a defect in the relatives of patients with that defect suggests a genetic factor in the etiology, since it is hard to conceive of a purely environmental influence which would affect uncles, aunts, and cousins of an affected person oftener than other members of the community. Failure to fit any regular Mendelian pattern indicates either that the genetic situation is extremely complicated or that the defect is determined by an interaction of genetic and environmental factors.

The congenital defects due to maternal immunization by fetal antigens may fall into the former group (a complicated genetic situation), although nongenetic factors have not been entirely ruled out. Erythroblastosis fetalis and related conditions are the outstanding examples of defects due to isoimmunization. It has been postulated that other conditions might also fall into this class.[27] Contrary to earlier indications, however,[28] it has recently been shown that Rh-antagonism plays no part in nonspecific mental deficiency,[29] and to our knowledge no other congenital defect has shown evidence of being due to isoimmunization.

The idea of a genetical-environmental interaction to account for some types of congenital defect is favored by the rather sparse evidence from twins. In cases of Mongolism,[30] hypertrophic pyloric stenosis,[31] and clubfoot,[25] for instance, in which at least one twin has the defect, the other also has it more frequently when the twins are monozygotic than when they are dizygotic. This excess of concordant cases in the genetically identical group suggests a genetic origin, but the fact that some

24. Fogh-Anderson, P.: Inheritance of Harelip and Cleft Palate, Copenhagen, Arnold Busck, 1942.

25. Böök, J. A.: Hereditas **34**:289, 1948.

26. Böök, J. A., and Rayner, S.: Am. J. Hum. Gen. **2**:61, 1950.

27. Kalmus, H.: Ann. Eugenics **13**:146, 1946.

28. Snyder, L. H.; Schonfeld, M. D., and Offerman, E. M.: J. Hered. **36**:9, 1945.

29. Böök, J. A.; Grubb, R.; Engleson, G., and Larson, C. A.: Am. J. Hum. Gen. **1**:66, 1949.

30. Warner, R.: Mongolism in One of Twins and in Another Sibling, Am. J. Dis. Child. **78**:573 (Oct.) 1949.

31. Powell, B. W., and Carter, C. O.: Arch. Dis. Childhood **26**:45, 1951.

genetically identical pairs are unlike with respect to the defect shows that nongenetic factors must be involved as well.

A great deal of work has been done in attempting to identify these nongenetic factors by study of the prenatal features of pregnancies resulting in defective offspring. For example, there is evidence from several sources that children of diabetic mothers run a slightly greater risk of having congenital defects than children of normal mothers,[32] although it is not known what particular aspect of the diabetic disorder is associated with production of defects. Placenta previa may also be associated with a slightly increased incidence of congenital defects,[20] and there is evidence that other types of maternal disorder, such as chronic systemic disease, uterine hemorrhage, and threatened abortions, occur more frequently than usual in the prenatal histories of Mongolian idiots.[18e] Murphy [12] found an abnormally high incidence of previous abortions or long periods of infertility in the mothers of his series of malformed infants. Incidence of defect shows a positive correlation with maternal age in the case of Mongolism,[33] hydrocephalus,[34] and the lethal defects of Murphy's series.[12] The month of conception was found to influence the incidence of anencephaly in an interesting study [34] which showed that offspring with anencephaly (but not those with spina bifida or hydrocephalus) were significantly more likely to be conceived in the second than in the other quarters of the year. Stevenson,[18c] on the other hand, reported that offspring with defects that were assumed on embryological grounds to take more than one month for their formation tended to be conceived in the fourth and first quarters.

Little is known of the mechanisms relating these factors to the resulting defects, and there are no data available which will allow one to measure the risk of a child being deformed when one of these factors is involved. To obtain such data, it is necessary to observe pregnant women who have had a threatened abortion, for instance, and determine how many of the resulting children are defective, rather than to start with the defective children and then determine how many of their mothers had threatened abortions.

To sum up the discussion so far, then, it has been pointed out that some congenital defects are clearly associated with changes at single gene loci. Others have a clear-cut environmental causation. A third group appears to be the result of an interaction between certain environmental factors, so far poorly defined, and particular genetic constitutions. Cases from each of these groups may be clinically indistinguishable.

## EXPERIMENTAL PRODUCTION OF CONGENITAL DEFECTS

Knowledge of the mechanisms of normal development and deviations therefrom has increased rapidly during the last 50 years, largely because of the studies of experimental embryologists on amphibian eggs.[35] The use of mutant genes to alter the normal course of development has enhanced our understanding of the embryogeny

32. Warkany.[18d] Hurwitz, D., and Irving, F. C.: Am. J. M. Sc. **194**:85, 1937. Joslin, E. P.; Root, H. F.; White, P., and Marble, A.: The Treatment of Diabetes Mellitus, ed. 7, Philadelphia, Lea & Febiger, 1940. Miller, H. C.: J. Pediat. **29**:455, 1946.

33. Penrose, L. S.: Ann. Eugenics **6**:108, 1934.

34. McKeown, T., and Record, R. C.: Lancet **1**:192, 1951.

35. (*a*) Gruenwald.[13d] (*b*) Needham, J.: Biochemistry and Morphogenesis, London, Macmillan Company, Cambridge University Press, 1942.

of the less accessible mammalian embryo.[36] New impetus was recently given to the experimental study of developmental deviations in mammals by the discovery that maternal infection with rubella may cause congenital defects in the offspring. Warkany [18d] has contributed an admirable review of the major developments in this fascinating subject up to 1947.

1. *Dietary Deficiencies.*—The field of maternal-fetal nutritional relationships is too large to be reviewed here. Suffice it to say that starvation does not seem compatible with mammalian reproduction, and that on a deficient diet the mother and fetus will compete for those constituents not present in quantities adequate for both. Whether mother or fetus gains the advantage depends on the particular constituent involved. Several authoritative reviews of the subject have appeared recently,[37] and the reader is referred to them for a thorough discussion of the problem.

(*a*) Vitamin A Deficiency: Perhaps the earliest experiment showing clearly that a specific maternal dietary deficiency could cause congenital defects in the offspring was that of Hale.[38] He raised pigs on a vitamin-A-free diet (supplemented with vitamin A during the later stages of pregnancy to allow completion of gestation) and found that the resulting offspring showed various defects, including anophthalmos, microphthalmos, harelip, cleft palate, and ectopic kidneys. Breeding tests with defective animals showed that the malformations were not associated with genetic changes. This is not surprising to geneticists, except perhaps those influenced by the dictates of the Communist party.

This discovery was confirmed and extended in a brilliant series of experiments by Warkany and his co-workers, who showed that female rats raised on a diet deficient in vitamin A were themselves retarded in growth and development and produced offspring which were reduced in size, did not survive, and showed a high incidence of malformation.[39] These included cleft palates,[40] malformations of the extremities,[39b] diaphragmatic hernias,[37g] and eye defects, such as fibrous dysplasia of the vitreous body, retinal coloboma, and aplasia of the ciliary body.[41] There were also malformations of the genitourinary tract, including fused or ectopic kidneys, undescended testes, hypospadias, and vaginal aplasia,[42] and cardiovascular defects, such as interventricular septal defects and anomalies of the aortic arch.[43]

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36. Schoenheimer.[13g] Needham.[38b] Waddington, C. H.: Organizers and Genes, London, Cambridge University Press, 1940; Growth, in Symposium of the Society for Experimental Biology, No. 2, London, Academic Press, Inc., 1948, p. 145.

37. (*a*) Warkany.[18d] (*b*) Burke, B. S.; Beal, V. A.; Kirkwood, S. B., and Stuart, H. C.: Am. J. Obst. & Gynec. **46**:38, 1943. (*c*) Burke, B. S., and Stuart, H. C.: Nutritional Requirements During Pregnancy and Lactation, J. A. M. A. **137**:119 (May 8) 1948. (*d*) Parsons, L. G.: Canad. M. A. J. **55**:327, 1946. (*e*) Huggett, A. St. G.: Brit. Med. Bull. **4**:196, 1946. Warkany, J.: (*f*) Vitamins & Hormones **3**:73, 1945; (*g*) Obst. & Gynec. Surv. **3**:693, 1948. (*h*) Burke, B. S.; Stevenson, S. S.; Worcester, J., and Stuart, H. C.: J. Nutrition **38**:453, 1949.

38. Hale, F.: J. Hered. **24**:105, 1933; Am. J. Ophth. **18**:1087, 1935.

39. (*a*) Warkany, J., and Nelson, R. C.: Science **92**:383, 1940. (*b*) Warkany, J.; Nelson, R. C., and Schraffenberger, E.: J. Bone & Joint Surg. **25**:261, 1943. (*c*) Warkany, J., and Roth, C. B.: J. Nutrition **35**:1, 1948.

40. Warkany, J.; Nelson, R. C., and Schraffenberg, E.: Congenital Malformations Induced in Rats by Maternal Nutritional Deficiency, Am. J. Dis. Child. **65**:882 (June) 1943.

41. Warkany, J., and Schraffenberger, E.: Congenital Malformations Induced in Rats by Maternal Vitamin A Deficiency: Defects of Eye, Arch. Ophth. **35**:150 (Feb.) 1946.

42. Wilson, J. G., and Warkany, J.: Am. J. Anat. **83**:357, 1948.

43. Wilson, J. G., and Warkany, J.: Am. J. Anat. **85**:113, 1949; Pediatrics **5**:708, 1950.

No definite conclusions were reached on how the nutritional deficiency produced its effect on the fetus, but the appearance of keratinizing metaplasia in certain epitheliums suggested that the deficiency in vitamin A was affecting the fetal tissues directly.[42] Mason,[44] on the other hand, found that in female rats bred on a vitamin-A-deficient diet there was injury to the uterine epithelium, followed by infection, placental necrosis, and interference with the nutritive supply of the fetus, resulting in death of a large number of embryos. Those that survived to the later stages of gestation or to birth showed various degrees of developmental retardation, but no congenital malformations.

Andersen [45] noticed a high incidence of congenital diaphragmatic hernia in the offspring of rats raised (for purposes other than the study of congenital defects) on a vitamin-A-deficient diet. This occurred in one of the strains used, but not in the other. In a constant environment, such a constitutional difference in susceptibility must be due to a difference in heredity. This sort of genetical-environmental interrelationship will be considered in more detail in a later section of this paper.

(*b*) Riboflavin Deficiency: Maternal deficiencies in other vitamins can also cause congenital defects in the offspring. Warkany found that rats bred on riboflavin-deficient diets gave birth to young with a variety of skeletal changes, such as shortening of the mandible, radius, ulna, tibia, and fibula, fused ribs, syndactylism, and cleft palate.[46] None of the soft-tissue defects found in the vitamin-A-deficient series occurred in these animals, and they were not reduced in size, suggesting that deficiencies in vitamin A and riboflavin differ in the mechanisms by which they cause embryonic defects. Here the importance of a borderline deficiency in producing defects was emphasized. When there was a little less than the critical level of riboflavin in the diet, gestation was not completed. A little more than the critical level gave normal offspring. The appearance of defects could be prevented by adding adequate amounts of riboflavin to the mother's diet before, but not after, the 13th day. These experiments suggested that riboflavin plays an important part in the differentiation of the membranous skeleton in rats and that this tissue at this time needs more riboflavin than at other times or than other embryonic tissues.[47] In mice, on the other hand, no skeletal defects were noted under similar conditions,[37g] providing another example of the importance of genetic factors in determining the effect of an environmental agent.

Giroud [48] confirmed the fact that the young of rats bred on a riboflavin-deficient diet might have cleft palates and/or shortened mandibles and minor skeletal abnormalities and measured the riboflavin levels in the maternal and fetal tissues of these animals.[49] He did not notice fusions of the fingers or bone "atrophies" such as Warkany described, and this observation was thought to suggest differences (presumably genetic) in "susceptibility" between the two strains.

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44. Mason, K. E.: Am. J. Anat. **57**:303, 1935.

45. Andersen, D. H.: Am. J. Path. **25**:163, 1949.

46. Warkany, J.: J. Pediat. **25**:476, 1944.

47. Warkany, J., and Schraffenberger, E.: J. Nutrition **27**:477, 1944.

48. Giroud, A., and Boisselot, J.: Arch. franç. pédiat. **4**:317, 1947; Rev. de stomatol. **49**:377, 1948.

49. Giroud, A.; Ettori, J.; Levy, G., and Boisselot, J.: Internat. Ztschr. Vitaminforsch. **21**:261, 1949. Giroud, A.; Levy, G., and Lefebvres-Boisselot, J.: Ibid. **22**:308, 1950.

(*c*) Other Deficiencies: Pantothenic acid deficiency had similar results,[50] causing the deficient rats to abort or to produce young showing anophthalmos, exencephalus, and localized hemorrhages coincident with deformities of the fingers. The incidence of these defects was not stated. The appearance of hydrocephalus in some of the offspring of rats raised on an "inadequate" diet,[51] may be due to a deficiency in folic acid. The prenatal effects of dietary deficiencies in copper, iodine, and vitamin D, not yet exhaustively studied, are reviewed by Warkany.[18d]

Doubtless, other nutritional deficiencies will be found to cause congenital defects as further work is done. Study of the embryological processes affected by specific deficiencies represents a new experimental tool which may contribute greatly to our understanding of fetal metabolism, as well as to our knowledge of developmental mechanics. To discover the extent to which these findings apply in human beings will be a more difficult problem, but with the increasing efficiency and scope of modern nutritional surveys it should be feasible to study the nutritional status of a large group of pregnant women and then see which ones give birth to defective children.

2. *Injurious Physical and Chemical Agents.*—(*a*) Irradiation: The effect of therapeutic irradiation of the pregnant woman has already been mentioned. Russell [52] and Warkany [18d] have reviewed the experimental studies on this subject. In pregnant mice and rats x-rayed during the later stages of gestation, the fetal damage was limited almost exclusively to the rapidly growing parts of the central nervous system.[53] Treatment at earlier stages produced a variety of defects, depending on the dose and the stage of gestation. In Warkany's series of x-radiated rats,[54] cleft palate appeared in offspring irradiated on the 10th, 12th, 13th, 14th, 15th, or 16th day of gestation, with the highest incidence on the 12th day. Fusion of the humerus and radius appeared only after irradiation on the 13th day but differed anatomically from the deformity produced by maternal riboflavin deficiency, in which the critical period also fell on the 13th day. In general, the large doses of radiation produced a higher incidence and greater severity of defects than the small doses.

The relation of the type of defect, the dose of x-rays, and the gestational stage at which radiation was applied has been studied in more detail by Russell,[52] using genetically homogeneous material. She found that single exposures of impregnated mice to x-radiation (200 r) in the preimplantation period (up to about five days) caused a high incidence of early fetal death but few abnormalities in the survivors. From about the 6th to the 13th days of gestation, radiation produced few fetal deaths and a high incidence of malformations. From the 14th day on, the embryos were not susceptible to radiation in doses up to 300 r. A variety of defects was produced, each one related to a particular time of irradiation. In some cases the defect appeared only in mice irradiated on one particular day—the "critical period." No defects had critical periods lasting more than three days. In general,

50. Boisselot, J.: Compt. rend. Soc. biol. **142**:928, 1948; Arch. franç. pédiat. **6**:225, 1949.

51. Richardson, L. R., and Hogan, A. G.: J. Nutrition **32**:459, 1946. Richardson, L. R., and DeMottier, J.: Science **106**:644, 1947. Richardson, L. R.: Proc. Soc. Exper. Biol. & Med. **76**:142, 1951.

52. Russell, L. B.: J. Exper. Zool. **114**:545, 1950.

53. Hicks, S. P.: Proc. Soc. Exper. Biol. & Med. **75**:485, 1950.

54. Warkany, J., and Schraffenberger, E.: Am. J. Roentgenol. **57**:455, 1947.

increasing the dose of radiation lengthened the critical period. In some cases the period of sensitivity could be related to the time that some relevant embryological process was proceeding rapidly, while in others no such relationship was apparent. Some types of defect resembled closely those produced by mutant genes. This, of course, does not imply that the radiation caused genetic changes which produced the defects but constitutes another example of the fact that genes and environmental agents may produce similar developmental deviations. Studies of this sort should add a great deal to our knowledge of developmental mechanisms in mammals.

(*b*) Hypoxia: Because of the frequency of threatened abortions and other maternal mishaps in pregnancies which subsequently produced certain types of congenital defect,[186] Ingalls was led to study the effect of maternal hypoxia on the developing embryo.[55] He found that exposures of pregnant mice to rarefied atmospheres for only five hours led to death or malformation of some embryos. Here again the result depended on the degree of hypoxia and the stage of gestation at which the insult was applied. Exposure to an atmosphere of 25,000 feet (7,620 meters) on the eighth day caused anencephaly in the offspring; exposure on the 14th day caused cleft palate.

(*c*) Trypan Blue: In an attempt to find an experimental parallel for the mechanism by which the rubella virus affects the fetus, Gillman [56] gave fortnightly injections of trypan blue to female rats and studied the effect on the offspring of these rats. A remarkable variety of malformations resulted from this treatment, including hydrocephalus, eye defects similar to those occurring in Warkany's vitamin-A-deficient series, spina bifida, short or absent tails, and (rarely) cleft lip and palate. Rats which had been given injections both before and during pregnancy showed a much higher incidence of defective offspring than those which received injections only during pregnancy. There seems to be a relation between the incidence of defects and the stage at which the animals were given the injections, but because of the peculiar nature of the experimental design this relation is not entirely clear. It is interesting, in view of our results with the administration of cortisone,[57] that the treated females showed gross enlargement of the adrenal glands. Further studies on the mechanism by which trypan blue produces its effects and its relation to stage of gestation are awaited with great interest.

(*d*) Nitrogen Mustard: Another noxious agent which when injected into pregnant rats produced malformations in the offspring is nitrogen mustard (methyl-*bis* or *tris* [2-chloroethyl] amine hydrochloride).[58] The defects so produced included cranial faults, underdeveloped jaws, cleft palate, absence or fusion of the toes, and short tail. Again there seemed to be a relation between stage of injection and type of defect; on the 13th day the anterior limbs were oftenest affected, whereas on the 14th day there were more posterior limb defects.

3. *Endocrine Factors.*—(*a*) Sex Hormones: Several workers have studied the effect on the embryo of injection of sex hormones into pregnant animals,[59] but

55. Ingalls, T. H.; Curley, F. J., and Prindle, R. A.: Anoxia as a Cause of Fetal Death and Congenital Defect in the Mouse, Am. J. Dis. Child. **80**:34 (July) 1950.

56. Gillman, J.; Gilbert, C., and Gillman, T.: South African J. M. Sc. **13**:46, 1948.

57. Fraser, F. C., and Fainstat, T. D.: Pediatrics, to be published.

58. Haskin, D.: Anat. Rec. **102**:493, 1948.

59. White, M. R.: Anat. Rec. **99**:397, 1947. Greene, R. R.; Burill, M. W., and Ivy, A. C.: Am. J. Anat. **65**:415, 1939; Anat. Rec. **74**:429, 1939. Turner, C. D.: J. Morphol. **65**:353, 1939.

interest has been focused largely on the development of the embryonic genital apparatus, and little attention has been paid to the effect of such treatment on other organs. The field has been reviewed by Moore,[60] who suggests that the developmental alterations in the embryonic reproductive tract produced by giving pregnant animals injections of sex hormones may be fundamentally comparable with those occurring in Warkany's vitamin-A-deficient series rather than a result of a specific action of sex hormones on sexual organs.

(*b*) Pituitary Hormones: An interesting example of the interaction of genetic and environmental factors in determining the presence of a congenital defect is supplied by Steiniger [61] (reviewed by Grüneberg [13c]), who worked with an inbred strain of mice in which about 10% of the animals had cleft lip and palate. When pregnant females were given an injection of an anterior pituitary preparation, the incidence of defects was raised to 17%. Possibly a different combination of dosage and timing might raise the proportion even more.

(*c*) Desoxycorticosterone Acetate: A report, of which only the abstract is available to us,[62] mentions the incidental observation of embryonic malformations in the young of pregnant ovariectomized hamsters given injections of desoxycorticosterone acetate. Whether the desoxycorticosterone acetate itself caused the defects is not yet clear. If so, this would provide some support for the suggestion of Selye [63] that excessive production of maternal adrenal cortical secretions might possibly cause congenital defects in the young.

(*d*) Cortisone: Our recent experiments [64] have demonstrated that cortisone when injected into pregnant mice will produce a high incidence of congenital defects in the offspring. It is not yet clear which of the many physiological actions of cortisone is responsible for its interference with embryonic development. It may act on the embryo secondarily by upsetting the mother's biochemical equilibrium and causing some abnormal metabolite to cross the placental barrier, or it may damage the placenta, thus interfering with embryogeny. Alternatively, it may act directly on the embryo, possibly through its catabolic effect on protein metabolism.[65]

In order to assess the clinical significance of this discovery, it will be necessary to know whether the naturally produced adrenal corticoids in excessive amounts can cause congenital defects as cortisone does. If so, the possibility exists that some of the forms of maternal insult which result in congenital defects may be regarded simply as forms of stress, causing the mother's adrenal gland to produce excessive amounts of cortisone-like compounds.

Our experiments showed that the dosages which produced defects were just below those which caused fetal resorption or expulsion. A similar situation has been noted with various other agents that interfere with embryonic development,

60. Moore, C. H.: J. Clin. Endocrinol. **10**:942, 1950.

61. Steiniger, F.: Ztschr. f. menschl. Vererb.- u. Konstitutionslehre **24**:1, 1940.

62. Tedford, M. D., and Risley, P. L.: Anat. Rec. **108**:596, 1950.

63. Selye, H.: The Physiology and Pathology of Exposure to Stress, Montreal, Acta, Incorporated, Medical Publishers, 1950.

64. Fraser and Fainstat.[57] Baxter, H., and Fraser, F. C.: McGill M. J. **19**:245, 1950. Fraser, F. C.: Canad. M. A. J. **64**:270, 1951.

65. Browne, J. S. L.; Johnson, L. G.; Schenker, V., and Venning, E. H., in Proceedings of the First Clinical ACTH Conference, edited by J. R. Mote, Philadelphia, The Blakiston Company, 1950, pp. 108-133.

including dietary deficiencies, radiation, and anoxia. It has been suggested that rubella is effective in causing congenital defects because it is not quite severe enough an insult to cause abortion. These observations emphasize the importance of obtaining reliable data on the incidence of congenital defects in offspring of pregnancies in which there was a threatened abortion.

Another interesting feature of these results was that the same dose of cortisone given at the same gestational stage produced very different proportions of cleft palates in the offspring of different strains of mice. Other examples of genetically determined differences in response to treatment have been referred to elsewhere in this review and emphasize the importance of using genetically controlled material in such studies.

## CONCLUSION

It has been emphasized by numerous workers that biological characteristics, including responses to experimental manipulation, are the result of an interaction between the genetic and the past environmental influences which make up the organism's constitution. Some characteristics are determined largely by genetic factors and others by environmental agents, while still others occupy an intermediate position. The fact that no one has been able to produce defects experimentally in 100% of the offspring of treated animals, even when using highly inbred material, shows that the production of such defects is influenced by environmental differences sufficiently subtle that they can occur within the maternal uterus. It is reasonable to suppose that this applies in human material as well. Clinically, therefore, the etiology of any given case of congenital defect (provided there is no obvious Mendelian pattern or environmental agent) must be attributed to a complicated interaction of genetic and environmental factors that can be defined only in statistical terms.

## SUMMARY

Etiological factors in the production of congenital defects are discussed. Some congenital malformations are clearly associated with changes at single gene loci. Others have a clear-cut environmental causation. A third group appears to be the result of an interaction between certain environmental factors, so far poorly defined, and particular genetic constitutions. Cases from each of these groups may be clinically indistinguishable.

A survey of the literature reviews the wide variety of environmental agents which, when applied to pregnant animals, will cause congenital defects in the offspring. These include dietary deficiencies in vitamin A, riboflavin, pantothenic acid, and folic acid; x-radiation; anoxia; injection of trypan blue, nitrogen mustard, and cortisone. In general the incidence and type of defect varies with the agent used, its dosage, the stage of gestation at which it is applied, and the genetic constitution of the animal involved.

# Abstracts from Current Literature

## Biochemistry; Bacteriology and Pathology

Induced Resistance to Bacitracin in Cultures of Staphylococcus Aureus. Joseph L. Stone, J. Infect. Dis. **85**:91 (July-Aug.) 1949.

The author determined rises in resistance of four strains of Staphylococcus aureus to bacitracin. Decrease in resistance was also studied. Resistance to bacitracin rose irregularly but steadily, and there was a tendency to level off at about 50 to 60 times the original titer. Loss of resistance to bacitracin was rapid if the resistant cultures were transferred daily to bacitracin-free nutrient broth; however, there was little or no decrease in bacitracin resistance following storage of the resistant cultures in the refrigerator up to 29 days.

Cross resistance studies with bacitracin-resistant strains showed either no change in penicillin resistance or a very slight decrease in resistance. Cross resistance studies with penicillin-resistant strains showed a greater bacitracin sensitivity as penicillin resistance rose and rise of bacitracin resistance as penicillin resistance dropped. The rise toward normal of bacitracin resistance did not occur, however, when penicillin resistance was decreased by maintaining the penicillin-resistant cultures in the refrigerator. The phenomenon of increased susceptibility to bacitracin of penicillin-resistant strains was not entirely specific, since in some instances the penicillin-resistant cultures showed also an increased susceptibility to mercuric chloride and copper sulfate.

Toomey, Cleveland.

Abderhalden's Reaction and Agglutination Following Use of Typhoid Antigen and Penicillin. U. Guelli, Pediatria **58**:511 (July) 1950.

In rabbits, the administration of penicillin, when given with typhoid antigen, does not interfere with the antibody formation or with Abderhalden's reaction.

Higgins, Boston.

## Metabolism; Infant Feeding; Milk and Other Foods

Factors Influencing Lobulo-Alveolar Development and Mammary Secretion in the Rat. Constance Curtiss, Endocrinology **45**:284 (Sept.) 1949.

There is no longer any uncertainty that the mammary gland is under hormonal control, but there is still much to be learned about the interaction of the specific hormones involved. It is felt that the experiments performed have shown that lobuloalveolar development as extensive as that seen in normal pregnancy in the rat mammary gland can be produced by estrogen and progesterone.

Jacobsen, Buffalo.

The Relation of the Amino Acid-Sugar Reaction to the Nutritive Value of Protein Hydrolysates. Leo Friedman and O. L. Kline, J. Nutrition **40**:295 (Feb. 10) 1950.

The work reported by Friedman and Kline affords direct evidence that the amino-acid-sugar reaction has a profound effect on the nutritive value of protein hydrolysates for the rat and that most of the dietary essential amino acids are made unavailable by the reaction. It is of special interest to note that relatively small changes in amino acid composition, as measured by microbiological assay, are associated with important changes in nutritive value for the rat. It appears, therefore, that there is an important difference between the animal and the microorganism with respect to the nutritional availability of the amino acids after their reaction with glucose. This raises the question of the applicability of the results of the microbiological assay of amino acids in assessing the nutritive quality of protein materials that have been subjected to heat treatment. It is suggested that the formation of an amino-acid-glucose complex that is not readily utilized by the animal may be the basis for the difference noted in the experiments reported here.

Fredeen, Kansas City, Mo.

THE EFFECT OF FAT LEVEL OF THE DIET ON GENERAL NUTRITION: V. THE RELATIONSHIP OF THE LINOLEIC ACID REQUIREMENT TO OPTIMUM FAT LEVEL. HARRY J. DEUEL JR., SAMUEL M. GREENBERG, CLARENCE E. CALBERT, EVELYN E. SAVAGE, and TOMOKO FUKUI, J. Nutrition **40**:351 (March 10) 1950.

The present experiments were undertaken in order to determine by new procedures whether fat contributes to nutrition other than as a source of the essential unsaturated acids and as a reservoir for meeting caloric needs. By the administration of the growth hormone, an attempt was made to accelerate the appearance of fat-deficiency symptoms in the rats. The injection of the growth hormone in such fat-deficient rats did not result in growth or cause death. When 20 mg. of linoleic acid was given as a supplement to the fat-deficient rats, a prompt response in growth resulted, which was not further augmented when the level was increased to 60 mg. a day. The injection of the growth hormone combined with the feeding of methyl linoleate to fat-deficient rats resulted in an immediate growth response, in contrast to the more tardy action of the linoleate alone. The administration of a 10% cottonseed oil diet to rats receiving linoleate at an optimum level resulted in further acceleration of growth. This may indicate that the oil possesses some effect other than that of linoleic acid; perhaps the results were dependent on an additive effect of other unsaturated acids or of fat itself.

FREDEEN, Kansas City, Mo.

THE IMPORTANCE OF THE DIETARY LEVEL OF FATS ON THEIR NUTRITIONAL EVALUATION. V. H. BARKI, R. A. COLLINS, C. A. ELVEHJEM, and E. B. HART, J. Nutrition **40**:383 (March 10) 1950.

The data presented demonstrate repeatedly that the rate of growth of rats was affected by changing the level of different fats in the diets. Raising the level of butterfat from 10 to 35% resulted in improved growth. On the other hand, improvement in growth was secured when the level of corn oil was decreased from 35 to 10%. In the cases of soybean oil and coconut oil, the influence of changing the fat level on the growth rate was not significant. These observations suggest that since different fats produce optimum growth at different levels of intake, a comparative evaluation of their nutritive merits based on only one dietary level may be misleading.

FREDEEN, Kansas City, Mo.

AMINO ACID IMBALANCE AND THE GROWTH REQUIREMENTS FOR LYSINE AND METHIONINE. C. R. GRAU and M. KAMEI, J. Nutrition **41**:89 (May 10) 1950.

As the protein of the chick's diet is increased, the lysine and methionine plus cystine requirements also increase but at a slower rate. Thus, a protein that contains 3.8% lysine will not satisfy the lysine requirement if it is fed at a level providing 20% protein in the diet but will be satisfactory at a dietary protein level of 30%. Attempts were made to simulate the effect of high protein levels by adding free amino acids to diets containing barely adequate amounts of lysine or methionine plus cystine. The growth depressions caused by these amino acid excesses were not correctable by raising the methionine level of the diet. When the diet contains 20% protein, the chick's requirements for methionine and cystine appear to be met by levels of approximately 0.5% and 0.3% of the diet, respectively, or 0.8% methionine alone.

FREDEEN, Kansas City, Mo.

CALCIUM RETAINED FROM ONE LEVEL OF INTAKE BY SIX ADOLESCENT GIRLS. FRANCES A. JOHNSTON, DORETTA SCHLAPHOFF, and THELMA MCMILLAN, J. Nutrition **41**:137 (May 10) 1950.

Six girls 13 and 14 years of age were maintained for nine weeks on a controlled diet, containing approximately 1 gm. of calcium a day. The mean retention was 281 mg., or 26% of the intake, which is the amount of calcium needed for girls of this age for building bone and other tissue.

FREDEEN, Kansas City, Mo.

ON THE AMOUNT OF TRYPTOPHANE IN THE SERUM PROTEIN OF WELL AND DYSTROPHIC INFANTS. P. BRUSA and M. NIGRO, Minerva pediat. **2**:155 (April) 1950.

The average percentage of tryptophane in the serum proteins of 40 normal infants and 20 normal adults was 1.41. The percentages in 43 dystrophic infants were found to fall within the limits for normal infants, with four exemptions. These four children were over one year of age, and the percentages of tryptophane averaged 1.96.

HIGGINS, Boston.

DEONTOLOGICAL ASPECTS OF LACTATION OF INFANTS. L. LASTE ECHETO, Acta pediat. españ. **97**:1 (Jan.) 1951.

In the words of a poet, the precepts of a theologian, and the reforming zeal of a pediatrician, Echeto discusses the ethical and scientific reasons for maternal breast feeding of infants.

He divides his paper into (1) the rights of the child to breast feeding; (2) growth and development and nutrition in breast-fed babies; (3) social reasons for not breast feeding; (4) physical reasons for abandoning breast feeding; (5) quotations from ancient doctors and philosophers regarding the subject, and (6) the part that the general practitioner can play in increasing the number of breast-fed babies.

The author also reports many of the ancient superstitions, one of which ascribes moral characteristics of famous men to the types of wet nurses they had as infants.

ALLEN, Santa Fe, N. M.

CONTRIBUTIONS TO THE KNOWLEDGE OF IRON AND COPPER METABOLISM IN CHILDHOOD: II. SERUM IRON AND COPPER LEVELS IN ACUTE AND CHRONIC INFECTIONS. W. BRENNER, Ztschr. Kinderh. **66**:14, 1948.

Continuing the study of serum iron and copper levels, the author investigated the changes in the serum levels of these two elements during infections and found regularly a reduction of the iron level and elevation of the copper level. The degree of these changes was not constant in acute infections, but in chronic infections the author made the following observations; In tuberculosis the changes of serum iron and copper are of similar degree in opposite directions, whereas in rheumatic fever the copper increase exceeds the iron decrease, and in congenital syphilis the opposite is the case. No relation could be found between serum iron and copper levels and hemoglobin content and erythrocyte count. The author suggests that serial observations of copper and iron levels in cases of these infections may give a better indication of the activity of the infectious process than some of the customary tests (erythrocyte sedimentation rate) and can be used as guides in therapy. The changes in the serum levels are to be considered as part of the defense apparatus of the organism against infections and are controlled by the diencephalon.

GLASER, Chicago.

## Hygiene; Growth and Nutrition; Public Health

SOME PRINCIPLES IN THE DEVELOPMENT OF SERVICES FOR CHILDREN WITH HEARING IMPAIRMENT. ARTHUR J. LESSER, J. Speech & Hearing Disorders **15**:101 (June) 1950.

Only a few hearing-conservation programs have thus far developed as medical care programs of the state boards of health and education departments. Most such departments carry out hearing testing programs. During the past generation the hearing of several million school children has been tested by audiometers. Knowledge needed to develop comprehensive programs of audiology is available, but its application is still limited to relatively few children in large cities. Individualized programs must be developed, with auxiliary workers being available for rehabilitation.

PALMER, Wichita, Kan.

MATERNAL, FETAL, AND INFANT MORTALITY IN LOUISIANA. JOHN S. LEMASSON and J. D. MARTIN, New Orleans M. & S. J. **103**:234 (Dec.) 1950.

Attention is drawn to the steadily diminishing maternal and infant mortality and to the problems still to be faced in maternal and infant care in Louisiana. Between 1925 and 1949 maternal death rates decreased from 11.1 to 1.2%. Rates for nonwhite women were three times

as great as for white. Improvement in rates was much greater in the white patients. Infant mortality rates declined from 91.1 to 37.7%. Nonwhite mortality rates were one and seven-tenths times the white in both 1925 and 1949.

The study shows that puerperal toxemias and speticemias are still the leading causes of maternal mortality, while hemorrhage, toxemias, and ectopic pregnancies still cause many deaths. Premature birth is the leading cause of infant deaths, and little progress has been made in this field in the state as a whole. The same is true of bronchopneumonia.

McGUIGAN, Evanston, Ill.

CAUSES OF DEATH 1943-1948. E. C. HALLETT, Clin. Rep. Adelaide Child. Hosp. **1**:227 (May) 1949.

Eight hundred two deaths over a period of five years are reviewed. The different causes of death were numerous. It was noted that congenital abnormalities caused one of every eight deaths. Of malignant tumors, brain tumors accounted for one-third. Only two deaths occurred from diabetic coma, and only two from kerosene poisoning.

McGUIGAN, Evanston, Ill.

HOSPITAL DEATHS IN NON-EUROPEAN CHILDREN. S. LEVIN, South African M. J. **24**:993 (Dec. 2) 1950.

Levin analyzes 557 deaths over a period of two years. Over-all mortality rates were 25% in 1948 and 17% in 1949. The high rate is due to several factors, most important being the fact that only very sick children were admitted to the hospital, and many were badly malnourished and many moribund when first seen. Commonest causes of death were pneumonia and gastro-enteritis, which accounted for one-third of the deaths. Twenty-six per cent of children over one month had tuberculosis somewhere in the body; of *32* patients with tuberculous meningitis, only two were still alive two years later.

McGUIGAN, Evanston, Ill.

THE LIVES OF CHILDREN IN SUBNORMAL HOMES. G. MAGGIONI and V. BACCHETTA, Arch. ital. pediat. e puericolt. **14**:187, 1951.

Maggioni and Bacchetta report on the general condition of children living in unsuitable dwellings (huts, basements, underground shelters, caves) in the poorest quarter of Rome. Some data are given about the high incidence of disease and about the nutritional state of the children; the necessity of improving the social and medical care and assistance is stressed.

FROM THE AUTHORS' SUMMARY.

CLIMATE IN SCHOOL HYGIENE. J. GARCIA-AYUSO, Acta pediat. españ. **88**:380 (April) 1950.

Garcia-Ayuso calls attention to the various types of climates, and says sanatoriums and convalescent facilities with adequate schooling should be made available for sick children in every province in Spain.

Tuberculosis, rheumatic fever, and hypothyroidism have too long been considered familial and are really environmental diseases. If removed from poor environments, children would grow and develop normally.

ALLEN, Santa Fe, N. M.

PUBLIC HEALTH EDUCATION IN URUGUAY. JAVIER GOMENSORO, Bol. Inst. internat. am. protec. infancia **24**:181 (June) 1950.

The author emphasizes that public health education in Uruguay has been offered in accord with elementary and high school programs since 1847. Advanced public health teaching acquires fundamental importance with the professorships of hygiene and of pediatrics and puericulture in the Faculty of Medicine. Furthermore, a specialized Office of Public Health Education was created in 1929 first as a dependency of the National Council of Hygiene, and afterwards constituted a Department of the Ministry of Public Health (Division of Hygiene).

The value of sanitary education, the methodology followed, and the importance of radio talks, particularly of educational motion pictures are discussed in this work. It also refers to the legislation for public health and to the organizations responsible for its enforcement.

Summing up, the author points out the different steps performed in public health education and makes known the methodical, harmonious, and integral work being done for a better life, based on health and human solidarity.

FROM THE AUTHOR'S SUMMARY.

OFFENSE OF FAMILY DESERTION. EVANGELISTA PEREZ DEL CASTILLO, Bol. Inst. internat. am. protec. infancia. **24**:172 (June) 1950.

The offense of family desertion is punished in almost all countries with the loss of liberty, according to the author. She believes that this procedure does not produce good results in practice. The prosecuted, deprived of liberty, cannot work to maintain his family, and, furthermore, as the action has been brought by his former companion, the mother of his children, he develops an idea of reprisal against the family and tries by all means not to keep up family maintenance. For contumacious fathers forgetful of their duties, the author proposes compulsory work in "pretransgressors camps," such as exist in Uruguay. Furthermore, the assignment to the camp should not be at the request of the injured party, but by official action, to eliminate the appearance of personal reprisal.

FROM THE AUTHOR'S SUMMARY.

INFANT MORTALITY RATE IN DENMARK. POVL HERTZ, Nord. med. **41**:899 (May 20) 1949.

The infant mortality rate in Denmark fell from 13.4% in 1901 to 4% in 1947. In comparison with Norway and Sweden, however, the mortality rate is rather high. In Sweden it is 2.5%, in Norway 3.5%, in Copenhagen 4%, in Stockholm 2.3%, and in Oslo 1.7%. The author believes that this higher infant mortality rate in Denmark is due to less breast feeding. In 1911-1916 only 1.6% of children were bottle-fed when they left the maternity hospital; in 1947 to 1948 16% were. The author believes that the propaganda for breast feeding is not sufficient at the maternity hospitals, and he recommends the attendance of pediatricians in maternity hospitals and the erection of children's hospitals over the country, as has been done in Sweden.

WALLGREN, Stockholm, Sweden.

WETZEL'S GRID AS COMPARED WITH THE HEIGHT AND WEIGHT OF 5,082 DANISH CHILDREN. JOHANNES DÖSSING, Ugesk. læger **110**:699 (June 6) 1948.

If the height-weight curves are looked upon as mathematically straight, there is about 40% agreement between the figures of Wetzel's grid and the actual values encountered in Danish children. At most a few per cent of the figures for Danish children correspond to those of the grid, which therefore is considered inapplicable to Danish conditions.

WALLGREN, Stockholm, Sweden.

## Prematurity and Congenital Deformities

CLEFT PALATE SPEECH: AN INTEGRATION OF RESEARCH AND CLINICAL OBSERVATION. EUGENE T. MCDONALD and HERBERT EUGENE BAKER, J. Speech & Hearing Disorders **16**:9 (March) 1951.

The authors suggest several hypotheses concerning cleft palate speech: 1. There is a critical point in the degree of closure of the nasal pharynx, which produces a characteristic balance between oral and nasal resonance. 2. At least some of the cleft palate patient's nasality results from a persistent habit of elevating the mandible and the dorsum of the tongue during speech. 3. The amount of nasal emission in cleft palate speech is related principally to mandibular and lingual positions and movement and only secondarily to the amount of closure of the nasopharyngeal port. 4. The same lingual and mandibular elevation is responsible for most of the cleft palate patient's articulatory errors. 5. An important part of the quality of cleft palate speech is the result of faulty phonation. Clinical material based on these hypotheses is outlined in detail.

PALMER, Wichita, Kan.

CORRECTION OF CLEFT PALATES BY DENTAL APPLIANCES. E. J. FREDERICKSON, Northwest Med. **50**:268 (April) 1951.

The importance of correcting palatal and facial deformities cannot be overemphasized. Although the general trend at the present time is toward surgical treatment of patients with congenital cleft palate, there remain a number of patients who have to be treated mechanically. In many instances the unrepaired cleft palate does not offer sufficient tissue for adequate reconstructive surgery. In other instances attempts at repair have failed or been incomplete. Appliances based on two distinct mechanical principles are described. One type is hinged and designed to be under the immediate control of the muscles of the soft palate. The second type is designed as a stationary appliance. The necessity for these appliances in addition to reconstructive surgery in many cases is made clear.

DOCTER, Seattle.

HOSPITAL FATALITY RATES FOR PREMATURE INFANTS. KATHERINE BAIN, JOHN P. HUBBARD, and MARYLAND Y. PENNELL, Pediatrics **4**:454 (Oct.) 1949.

As a part of a study of child health services, conducted partly by the American Academy of Pediatrics, information was secured from hospitals caring for 50 or more premature infants a year. Data collected were number of live births in the hospital and number of cases and number of deaths for premature infants born in the hospital with various birth weights and for premature infants born outside and admitted for care. In the eligible hospitals reporting (about one-half the total) some 600,000 births occurred in one year. The incidence of prematurity in these hospitals, classifying as premature all live-born infants weighing 2,500 gm. or less, was 6.1%.

From a smaller sample, where race was given, the incidence for white infants was 5.6% and for nonwhite 9.5%. The fatality rate, that is, death before discharge from the hospital, was 21.5% for the group born in the hospital. For those born outside the hospital and admitted for care, the rate was 36.6%. The close relation between survival and weight at birth is shown. For nonwhite infants the fatality rate was higher than for white infants. For the group born in the hospital the rate was 27.7% for nonwhite as contrasted with 24.5% for white, and for those born outside, 43.9% as contrasted with 31.5%.

FROM THE AUTHORS' SUMMARY.

CONGENITAL MALFORMATIONS IN ONE OF MONOZYGOTIC TWINS. J. EDGAR MORISON, Arch. Dis. Childhood **24**:218 (Sept.) 1949.

Two sets of twins with monochorionic placentas and placental vessel anastomoses are regarded as monozygotic twins. One of each set showed malformations affecting many different organs. Since the genetic inheritance of the malformed twin should be similar to that of its normal partner, it is suggested that the malformations arose from the arrest of normal development when the placenta of one twin was at some environmental disadvantage in obtaining nutrition from the uteroplacental site for a short period early in intrauterine life. The abnormalities found were consistent with some such nonspecific influence causing an arrest of development of those structures whose formation might be in a critical stage at about the sixth and the fourth week respectively.

KELLY, Milwaukee.

PARTIAL HEMIHYPERTROPHY OF RIGHT LEG. J. R. D. WEBB, Proc. Roy. Soc. Med. **42**:77 (Feb.) 1949.

A girl of 22 months showed hypertrophy of the right leg only. In every other respect she was normal.

WILLIAMSON, New Orleans.

RETROLENTAL FIBROPLASIA. HERBERT KAYE and A. M. RUDOLPH, South African M. J. **24**:1089 (Dec. 30) 1950.

Two cases of retrolental fibroplasia are described, and the literature is reviewed.

McGUIGAN, Evanston, Ill

THE BONNEVIE-ULLRICH SYNDROME IN A PREMATURE INFANT BORN AT THE SIXTH MONTH OF PREGNANCY (CYST OF THE NECK WITH CLUBFEET AND CLUBHAND). M. REINIGER, Ann. pædiat. **176**:32 (Jan.) 1951.

A fetus was examined anatomically; it presented a huge fluid-filled cyst in the nape of the neck, clubfeet, and a clubbed left hand. There were no malformations of the internal organs and eyes. Because of these findings the fetus was thought to show the Bonnevie-Ullrich syndrome. Difficulties in the diagnosis were created by the age of the fetus (6 months) and the third-degree maceration, which in similar cases of malformations made the diagnosis impossible.

This case shows great similarities with the one described by Grunwald and Kornfeld, but the lymphatic tissue which they observed in the walls of the cysts was not found in the histological slides in the present case. The author could not say whether there was a hereditary causation, as there was nothing in the history pointing to it. On the other hand, the pregnancy was uneventful, and so no exogenic damage to the embryo could be assumed.

FROM THE AUTHOR'S SUMMARY.

CONGENITAL BRACHYESOPHAGUS (PARTIAL THORACIC STOMACH) ASSOCIATED WITH ANEMIA. M. CORDEIRO and C. DA ROCHA PINTO, Helvet. paediat. acta **5**:532, 1950.

A case is presented of short esophagus with partial thoracic stomach, with the clinical history, roentgen examination, esophagoscopic and laboratory findings, in a child 2 years of age whose only symptom was severe anemia of hypochromic, microcytic type.

There were other etiological factors contributing to this severe anemia, which are briefly discussed, the principal one being the congenital lesion found at the roentgen examination.

The therapeutic measures confirmed this diagnosis as the blood picture showed much improvement, although it never returned entirely to normal.

Among the etiological factors of hypochromic, microcytic anemia in children, we must consider the possibility of short esophagus with thoracic stomach, even in absence of other symptoms, particularly gastric manifestations, as in our case.

FROM THE AUTHORS' SUMMARY.

GARGOYLISM, FORME FRUSTE. K. E. SJOLIN, Acta pædiat. **40**:165 (March) 1951.

After briefly reviewing previously reported cases of gargoylism, the writer describes a 10-year-old boy of normal intelligence showing proportioned dwarfism, a large monstrous head with open sutures and fontanels, stumpy hands and feet with clubbed distal phalanges, and a coarse, wrinkled skin on the fingers. X-ray examination showed well-marked osteosclerosis of the skull, vertebral column, and metaphyses and deficient ossification in the distal phalanges. The diagnosis is discussed, and the case is interpreted as one of gargoylism (forme fruste).

FROM THE AUTHOR'S SUMMARY.

PHYSIOLOGIC AND CHEMICAL RESPONSE OF PREMATURE INFANTS TO OXYGEN-ENRICHED ATMOSPHERE. BRUCE D. GRAHAM, HELEN S. REARDON, JAMES L. WILSON, MAKEPEACE U. TSAO, and MARY L. BAUMANN, Pediatrics **6**:55 (July) 1950.

Arterial blood studies were performed on 44 premature infants while they were in atmosphere and greater concentrations of oxygen. Analyses were made for oxygen content, oxygen capacity, and hematocrit reading. Concomitantly, plethysmographic studies were made on 29 occasions. Results were as follows:

1. Only seven (25%) of the premature infants studied breathed regularly in atmosphere; the remaining infants breathed with some degree of periodicity (44%) or with complete irregularity (30%).

2. As the concentration of oxygen being breathed was raised, more of the group shifted to a regular type of respiration, until in 75 to 85% oxygen, 88% of the group breathed with a regular type of respiration.

3. (*a*) The percentage of arterial oxygen saturation of the group averaged 93% in atmosphere, 96% in 30 to 55% oxygen, 100% saturation in 70 to 79% oxygen being breathed, and 102%

in 80 to 89% oxygen. (*b*) In atmosphere, when compared on the basis of age, the younger group (1 to 14 days) had essentially the same arterial group saturation as the older group (14 to 65 days). In an atmosphere of 70 to 90% oxygen, the saturation of the younger group increased to 102%, while that of the older group rose to 100%. (*c*) When compared on body weight basis, the 0.9 to 1.3 kg. group increased the arterial oxygen saturation of 85% in atmosphere to 102% when 70 to 85% oxygen was administered; the 1.3 to 1.8 kg. group, 93 to 101%; the 1.8 to 2.3 kg. group 90 to 100%.

(It is noted that either on the basis of age or body weight the group with higher hematocrit reading attained higher arterial oxygen saturation when 70 to 85% oxygen was administered than the group with lower hematocrit reading.)

4. (*a*) A statistical analysis of the respiratory records revealed an average rise of 30% in minute volume when 30 to 40% oxygen was administered, this rise being significantly maintained as higher concentrations (to 90%) of oxygen were administered. (*b*) An average significant rise in respiratory rate of 30% was noted when 30 to 40% oxygen was administered, which slowly fell to the original rate level as oxygen administered was increased to 80 to 90% concentration. (*c*) Consequently, the tidal volume (volume per respiration) gradually increased to 30% above the level in atmosphere as oxygen administered was increased to 80 to 90% concentration.

FROM THE AUTHORS' SUMMARY.

ABSORPTION OF FAT AND VITAMIN A IN PREMATURE INFANTS: I. EFFECT OF DIFFERENT LEVELS OF FAT INTAKE ON RETENTION OF FAT AND VITAMIN A. SOLEDAD MORALES, ARTHUR W. CHUNG, J. M. LEWIS, ANGELINA MESSINA and L. EMMETT HOLT JR., Pediatrics **6**:86 (July) 1950.

Eight premature infants manifesting steatorrhea were placed on diets containing low and high amounts of fat in order to ascertain how economically the premature infant could utilize large amounts of fat. At the same time the effect of administering large amounts of fat on the vitamin A absorption of premature infants was investigated. The results of these studies indicated that, in spite of steatorrhea, the percentage of fat absorbed was essentially the same whether the diet contained high or low amounts of this food. Thus, the net absorption of fat was correspondingly higher following the use of a high-fat diet. The absorption of vitamin A was approximately the same following the low or high fat regimen.

The finding that relatively high-fat diets given to premature infants not only result in better fat retention but are also well borne clinically suggests that the currently advocated restriction of fat in these subjects is unnecessary and possibly undesirable.

FROM THE AUTHORS' SUMMARY.

## Newborn

PERFORATION OF GASTRIC ULCER ASSOCIATED WITH INTRACRANIAL HEMORRHAGE IN NEWBORN INFANT. C. GOTTLIEB, F. CHU, and H. SHARLIN, Radiology **54**:595 (April) 1950.

The authors report a case of perforated gastric ulcer in a 24-hour-old boy. Free air was present beneath the diaphragm. At surgery a hole 3 cm. in diameter was found to be surrounded by a necrotic ulcer. The patient died 16 hours later. At necropsy an intracranial hemorrhage due to a tear in the tentorium was found. The authors' hypothesis is that, since melena in infants may be attributable to an intracranial lesion, the findings in their case must be considered an example of such a relationship.

ANSPACH, Chicago.

MYASTHENIA GRAVIS OF THE NEWBORN. A. K. GEDDES and H. M. KIDD, Canad. M. A. J. **64**:152 (Feb.) 1951.

Myasthenia gravis in the newborn infant of a mother also suffering from the disease is presented. Nine cases of newborn myasthenia gravis had been previously reported in the literature. Two other similar cases are described. The authors' patient recovered after 36 days of treatment with neostigmine (prostigmine®). It is believed that this transient myasthenic syndrome occurs only in infants born of myasthenic mothers.

MCGUIGAN, Evanston, Ill.

BROMSULPHALEIN EXCRETION IN THE NEWBORN. P. L. MOLLISON and MARIE CUTBUSH, Arch. Dis. Childhood **24**:7 (March) 1949.

Sulfobromophthalein (bromsulphalein®) injected into infants a few hours after birth is removed from the plasma far less rapidly than in adults. This finding is most probably to be explained by an immaturity of the excretory function of the liver.

KELLY, Milwaukee.

LIVER FUNCTION IN NEWBORN INFANTS. SIMON YUDKIN and SYDNEY S. GELLIS, Arch. Dis. Childhood **24**:12 (March) 1949.

Eighty-three sulfobromophthalein sodium excretion tests have been carried out on full-term infants from 8 to 216 hours old. The younger infants showed greater retention of dye than did infants over 4 days of age; the results are statistically highly significant. The infants over 4 days old showed greater retention than that reported for adults given equivalent amounts of dye. There was no correlation between the amount of dye retention and the level of serum bilirubin or between the amount of dye retention and the weight of the infant.

KELLY, Milwaukee.

THE EFFECT OF TOXAEMIA OF PREGNANCY UPON THE FOETUS AND NEWBORN CHILD. AGNES A. BRASH, Arch. Dis. Childhood **24**:107 (June) 1949.

The incidence of stillbirth and the occurrence of neonatal death have been found to be higher in infants born at term to toxemic women than in the full-term infants of nontoxemic women delivered in the same hospital. The principal cause in both cases is the greater liability to asphyxia resulting from antepartum hemorrhage and placental infarction. No postmortem evidence has been found to support the view that toxic changes in the fetus occur as the direct result of maternal toxemia.

A higher incidence of neonatal edema was found in the full-term infants of toxemic mothers than in controls. In a small series of cases albuminuria on the third day of life occurred less frequently in the infants of toxemic mothers than in controls. The incidence of premature labor was found to be significantly higher in toxemic women than in nontoxemic women delivered in the same hospital during the same period. The stillbirth rate and neonatal mortality rate of premature infants born to toxemic women were lower than those of premature infants born to nontoxemic women in the same hospital. Lactation of toxemic women was less satisfactory than that of nontoxemic controls.

KELLY, Milwaukee.

PLACENTA PERMEABILITY AND ANTIBODY VARIETIES IN RHESUS IMMUNIZATION. L. DE KROMME and L. A. M. VAN DER SPEK, Maandschr. Kindergeneesk. **18**:130 (No. 3-4) 1950.

There are individual differences in placenta permeability for antibodies. Placenta permeability is one of the factors determining the severity of the symptoms in the erythroblastotic child. It plays a more important role in those cases of erythroblastosis fetalis caused by large molecular antibodies than in those due to antibodies of small molecular structure.

The so-called monovalent, small-molecular Rh antibodies pass the placental barrier more easily than the large-molecular, so-called bivalent Rh antibodies.

Besides placenta permeability, another factor plays a role in explaining the so-called discrepancy between the titer of the antibodies in the serum of the mother and the symptoms in the child: the existence of highly active antibodies of even smaller molecular structure, which cannot be detected in the conglutination test. It is possible to gain an approximate insight into the amount of these antibodies present in an antiserum by determining the titer of the indirect Coombs test, the titer of the conglutination test, and their quotient.

FROM THE AUTHORS' SUMMARY.

SEROLOGICAL INVESTIGATIONS OF ANTI-HUMAN-GLOBULIN SERUM (SERUM OF COOMBS) WITH SPECIAL REFERENCE TO PATHOGENESIS OF ERYTHROBLASTOSIS FETALIS. J. J. VAN LOGHEM, Maandschr. Kindergeneesk. **18**:115 (No. 3-4) 1950.

Three different methods of production of anti-human-globulin serum are described. The highest titers are obtained with the injection of gamma-globulin. The high-titered anti-human-globulin serums cause prozone effect with sensitized red cells.

This prozone effect was first observed in three cases of acquired hemolytic anemia. It could be proved that the occurrence of this prozone phenomenon depends on the degree of sensitization of red cells by incomplete antibodies.

The cause of the prozone effect may be explained by two different theories. More detailed information will be published later.

It may be stated that only after prolonged immunization of rabbits does the prozone effect occur; after short immunization with gamma-globulin the same high titers are obtained, but without the production of a marked prozone effect.

The heterophile antibodies in the rabbit serum are destroyed by heating the serums for one to two hours at 63 C. This means that the absorption procedure with A-B-O cells to eliminate the heterophile antibodies is unnecessary.

In order to prevent diagnostic failures by the application of the direct anti-human-globulin test, it will be advisable to investigate the red cells with serial dilutions of the anti-human-globulin serum.

A method to estimate the degree of sensitization of red cells in erythroblastosis fetalis is described. It could be stated that often the red cells are weakly sensitized, even if the child is severely diseased. This can be explained in the light of the following findings:

A great difference in titer of incomplete antibodies between the maternal serum and the umbilical-cord blood is often found, while at the same time the red cells of the child are weakly sensitized. This corresponds with the investigation of van Bolhuis, who stated that there is a direct fixation of Rh antibodies on Rh antigens in the different tissues.

This leads to the conclusion that the results of exchange transfusion will be better if the antigen-antibody reaction is mainly restricted to the red cells, and less successful if tissues such as liver, spleen, and brains are involved.

FROM THE AUTHOR'S SUMMARY.

## Acute Contagious Diseases

IMMUNIZATION IN EARLY CHILDHOOD. LOUIS W. SAUER, Illinois M. J. **97**:73 (Feb.) 1950.

Simultaneous active immunization against diphtheria, tetanus, and pertussis is effective. Three monthly doses of alum-precipitated diphtheria and tetanus toxin are preferred. The best age for the initial dose is the sixth month of life. When earlier immunization is attempted, it should not be begun before the third or fourth month of life, and four monthly doses are recommended. A booster dose of alum-precipitated diphtheria and tetanus toxin is recommended before school attendance, and after presumed exposure of the previously immunized. Smallpox vaccination should not be performed until completion of basic immunization against diphtheria, tetanus, and pertussis. Immunization against scarlet fever, typhoid, and tick fever should be performed when indicated.

FROM THE AUTHOR'S SUMMARY.

FOLLOW-UP STUDY OF PERTUSSIS IN INFANCY. RANDOLPH K. BYERS and NICHOLAS D. RIZZO, New England J. Med. **242**:887 (June 8) 1950.

The authors studied 39 children admitted to Children's Hospital of Boston with whooping cough with and without complications. Their ages ranged from 3 weeks to 2 years. The cases of 4 were discarded because of evidence of preexisting cerebral defects, leaving 35 children for consideration. Of these, 23 had uncomplicated pertussis, 8 had complicating pneumonia, 4 had complicating encephalopathy, and 1 had both.

Twenty-six children recovered without any apparent developmental abnormality, either physical or mental, the follow-up information spanning the period from 3 years to school age. Nine children presented evidence of emotional and intellectual difficulties which in 6 were severe

enough to produce incompetence which had persisted. In the other 3 children, the developmental damage was severe but temporary. The case histories of these 9 children are given in detail. No asthma or bronchiectasis was found.

Although the authors presented evidence in an earlier paper that pertussis vaccine may induce encephalopathy in rare instances, they believe that the risks of the disease probably outweigh those incurred in the course of prophylactic immunization against pertussis.

WHEELOCK, Denver.

POLYIOMYELITIS IN THE ARCTIC. J. D. ADAMSON, J. P. MOODY, A. F. W. PEART, R. A. SMILLIE, J. C. WILT, and W. J. WOOD, Canad. M. A. J. **61**:339 (Oct.) 1949.

A widespread epidemic of poliomyelitis among Eskimos in the Eastern Arctic of Canada occurred in the winter of 1948-1949. The epidemic was of unprecedented severity. In one area it killed 5% of the population and paralyzed an additional 14%. Spread appeared to be through clinically well carriers. All ages above 3 years were involved. The spread of cases indicated a complete lack of immunity except in the first three years. The cases were almost all of the spinal type, with almost no bulbar or cerebral involvement. The epidemic features indicate that in a nonimmune community poliomyelitis behaves like any acute infectious disease.

MCGUIGAN, Evanston, Ill.

PULMONARY COLLAPSE IN PERTUSSIS. DAVID P. NICHOLSON, Arch. Dis. Childhood **24**:29 (March) 1949.

The literature relating to pertussis and bronchiectasis has been reviewed. It has been concluded that pulmonary collapse is a common feature of pertussis and that if reexpansion does not occur within nine months, it is unlikely to do so, and bronchiectasis may supervene. Treatment in these cases must be prolonged and efficient. Postpertussis pulmonary collapse is often still unrecognized.

KELLY, Milwaukee.

WHOOPING COUGH—PYRIBENZAMINE IN ITS SYMPTOMATIC TREATMENT. J. HELMAN, South African M. J. **23**:962 (Nov. 26) 1949.

In four cases of whooping cough tripelennamine (pyribenzamine®) was used, and the patients seemed to show a striking reduction in the number and frequency of paroxysms.

MCGUIGAN, Evanston, Ill.

LIMITATIONS OF ANTIBIOTIC THERAPY IN FULMINATING MENINGOCOCCUS MENINGITIS. J. CATHALA, R. LAPLANE, CONTAMIN, and VASEF, Presse méd. **57**:181 (Feb. 26) 1949.

A 6-year-old girl was suddenly taken ill with fever, chills, and vomiting. A few petechiae appeared on the trunk. Shock developed and masked any neurological changes. The cerebrospinal fluid was purulent, but cultures were sterile. The child died on the third day, despite heroic treatment with penicillin, sulfonamides and streptomycin. At autopsy the brain showed congestion but no purulent process. The adrenals were not hemorrhagic.

The authors suggest that in such cases the infection itself is cured by the antibiotic therapy, but the physiological pathologic change produced by the disease does not respond to these agents, and a lethal process is set up.

DAFFINEE, Melrose, Mass.

TREATMENT OF VACCINE VIRUS TO PREVENT SECONDARY COMPLICATIONS. G. RAMON, R. RICHOU, and J. P. THIERY, Presse méd. **57**:245 (March 19) 1949.

Ramon has developed a vaccine virus which is attenuated and free from other pathologic organisms. This is done by the use of a solution of formaldehyde (formalin®) and heat. The use of this vaccine should eliminate the complications of routine smallpox vaccination.

DAFFINEE, Melrose, Mass.

PENICILLIN TREATMENT IN SCARLET FEVER. P. GIRARDET, M. ROHNER, and H. ZELLWEGER, Helvet. paediat. acta **5**:101 (May) 1950.

Large doses of penicillin were given in a seven-day therapeutic trial to 355 patients suffering from scarlet fever. Three different methods of administering the drug were tested and the following was found to be the most satisfactory: twice daily an intramuscular injection of 100,000 to 120,000 units of penicillin G sodium.

The patients were treated in isolated groups of two to four children. At the end of the penicillin treatment the children were transferred to fresh and thoroughly cleaned cubicles, where they received a change of clothing and bedding. The children were kept in the hospital for three weeks.

Swabs taken from these children after the treatment showed that the number of carriers harboring hemolytic streptococci (type A) in the nose or nasopharynx had been reduced to approximately the number commonly found among healthy children.

Children who yielded swabs positive for streptococci after penicillin treatment were given a second full-course treatment, their roommates receiving at the same time a course on a reduced scale.

The incidence of remissions after this treatment was 0.87% and that of return cases 0.87%. Complications occurred in 9.3% of the cases, though none were serious.

It is recommended that hospitalization should not exceed 14 days, provided a swab negative for pathogens is obtained, and the period of isolation on returning home can be reduced to 14 days.

FROM THE AUTHORS' SUMMARY.

PERTUSSIS ENCEPHALOPATHY. H. ZELLWEGER and R. STEINEGGER, Helvet. paediat. acta **5**:139 (May) 1950.

This is a short study of encephalosis following whooping cough. In one case, the disease presented the picture of Feer's disease of short duration, combined with convulsions.

In the blood, there is nearly always a high leucocytosis; in the cerebrospinal fluid, a moderate pleocytosis, a moderate increase of the proteins, and an elevated sugar content.

Family histories of neurasthenia, nervousness, migraine, and tendency to fainting are common findings.

The patients themselves are nervous, with a certain lability of mind and feelings and numerous signs of incoordination of the vegetative nervous system. In some cases these signs were present before the encephalosis was observed, but in most they were found at the follow-up examinations of the patients. Signs of a lability of the vasomotor system were especially striking.

The appearance of encephalosis does not depend on the severity of the preceding whooping cough. Therefore, the author thinks that for the appearance of encephalosis after whooping cough, besides the presence of pertussis endotoxins, a constitutional factor, consisting in a lability of the vegetative nervous system, especially of the vasomotor system, is necessary.

FROM THE AUTHORS' SUMMARY.

TREATMENT OF PERTUSSIS WITH HYPERIMMUNE HUMAN SERUM. J. PROCHAZKA, A. TRAPLOVA, L. MICOCHVA, and V. KUMBERA, Helvet. paediat. acta **5**:528, 1950.

Eighty-nine patients with whooping cough at the State District Hospital, Bulovka, Prague, were treated with hyperimmune human antipertussis serum produced there. The mortality was lowered from 42% during 1941 to 1946 to 29% among those patients treated with hyperimmune serum.

FROM THE AUTHORS' SUMMARY.

TREATMENT OF PERTUSSIS WITH CHLORAMPHENICOL AND AUREOMYCIN. F. BUSER, Schweiz. med. Wchnschr. **81**:282 (March 24) 1951.

Chloramphenicol and aureomycin were given by mouth in the spasmodic stage of pertussis. In some cases the bitter chloramphenicol was given by rectum or by inhalation. When the particles are sufficiently small, the bitter taste becomes minimized. This method of administration is promising. Chloramphenicol was given to 16 children 1 to 4½ years of age. In two

other children 4 and 5¼ years of age treatment was by inhalation. Aureomycin was given to 4 infants, to 11 children 1 to 4 years of age, and to 5 aged 4 to 6 years. In some cases hyperimmune serum was given in addition. In severely toxic cases the serum treatment should be given. It can be combined with use of the antibiotic drugs. Both chloramphenicol and aureomycin proved effective. The author recognizes that the number of observations is too small for final evaluation.

AMBERG, Rochester, Minn.

EARLY TREATMENT OF POLIOMYELITIS AND THE FOLLOW-UP TREATMENT OF ITS RESIDUALS. D. GOTTI and P. NICOLAJ, Clin. pediat. **31**:595 (Nov.) 1949.

In the 10-year period 1939 to 1948, 2,038 patients with poliomyelitis were treated in the Antipoliomyelitis Center in Bologna. Epidemics occurred in the years 1939 (558 cases), 1941 (370 cases), and 1946 (271 cases); in 1944 only 38 new cases were seen. Of the cases, 29% were from the cities and 71% from the country districts; 79% of the cases occurred in the months of May to October. The age peak (31%) was 2 years. There were 61 deaths, 70% being in males, although only 53% of the total cases were in males. Early treatment resulted in excellent recovery of muscle function in 48% of the cases, while delayed treatment resulted in recovery in only 21%. Physical therapy and electrotherapy are stressed; immobilization is not used. Charts for the following of progress in muscle function are demonstrated.

HIGGINS, Boston.

DISEASE OF HEINE-MEDIN IN ADOLESCENTS AND ADULTS IN ITALY. G. LENZI and A. DEGLI ESPOSTI, Clin. pediat. **31**:623 (Nov.) 1949.

In a study of cases of poliomyelitis seen in the Antipoliomyelitis Center in Bologna, it was noted that bulbar symptoms were more frequent in adolescents and adults than in the children; also the paralyses were more diffuse. The mortality rate was higher in the adult cases.

HIGGINS, Boston.

FROEHLICH'S SYNDROME FOLLOWING POLIOMYELITIS. A. DEGLI ESPOSTI, Clin. pediat. **31**:635 (Nov.) 1949.

The case of a child of 5 years is reported in which adiposogenital dystrophy (Froehlich's syndrome) became manifest after a relatively mild attack of poliomyelitis; the syndrome is possibly the result of encephalitic changes from the poliomyelitis virus. Although the literature records few if any endocrinopathies following poliomyelitis, it is not uncommon to observe patients who have had that disease becoming unduly obese.

HIGGINS, Boston.

STUDY OF THE Na, K, AND Cl IONS AND THE PROTEIN OF THE BLOOD IN SOME INFECTIOUS DISEASES OF CHILDREN. C. STICCA, Lattante **20**:343 (June) 1949.

In diseases with toxemia present, such as diphtheria and scarlet fever, it was noted that there was an increase in the potassium and a decrease in the sodium and chlorine ions of the blood serum; the serum albumin increased and the serum globulin decreased in amount. No changes were found in the blood serum in cases of chickenpox.

HIGGINS, Boston.

ABSORPTION OF METHIONINE IN HEALTHY SUBJECTS AND IN SCARLET FEVER PATIENTS WITH LIVER INVOLVEMENT. A. LORENZELLI, U. MONDOLFO, and V. CAMBONI, Minerva pediat. **2**:478 (Oct.) 1950.

Methionine (2% solution, 0.02 gm. per kilogram of body weight) was injected intravenously. Blood withdrawn three hours after the injection had a higher level of methionine in two-thirds of the patients with scarlet fever and liver dyscrasia than in the healthy subjects. Methionine injections, in addition to aiding in the diagnosis of liver dysfunction, have some therapeutic value in liver disease.

HIGGINS, Boston.

AUREOMYCIN AND CHLOROMYCETIN IN THE TREATMENT OF PERTUSSIS. L. BARBERA and G. MARCHESE, Pediatria **58**:177 (March) 1950.

Very satisfactory therapeutic results, especially with infants, followed the giving of either aureomycin or chloramphenicol (chloromycetin®) to 18 children with pertussis. The dose given was 50 mg. per kilogram of body weight. The best results were in those children treated in the early stages of the disease.

HIGGINS, Boston.

CLINICAL CONSIDERATIONS OF THE POLIOMYELITIS EPIDEMIC IN AND AROUND HOF. HEINZ LAUBMANN, Med. Klin. **46**:324 (March 16) 1951.

During the fall of 1948, 160 cases of poliomyelitis were seen in an area (in and around Hof) in Bavaria. In some children the disease developed after some trauma and in one after tonsillectomy and adenoidectomy. In 15 cases eosinophile counts up to 23% were noted. In 21 cases paralysis of the large intestine and bladder was noted, though it was of short duration. In 40% manifestations of involvement of the diencephalon were seen. It is recommended that the patients be treated as early as possible in hot baths of a temperature higher by 1 degree C. than the body temperature. This has to be done in the preparalytic stage.

AMBERG, Rochester, Minn.

THE EPIDEMIOLOGY OF POLIOMYELITIS. S. KRAUTER, Wien. klin. Wchnschr. **61**:803 (Nov. 18) 1949.

An epidemic of 81 cases of poliomyelitis, of which 40 included hospital admission, is analyzed.

AMBERG, Rochester, Minn.

COMPLEMENT FIXATION TEST IN CERTAIN AND SUSPECTED CASES OF MUMPS MENINGITIS. VERA OLDFELT, Nord. med. **38**:885 (April 30) 1948.

Complement fixation tests for mumps antibody were performed in 40 cases of mumps meningoencephalitis and some cases of "aseptic meningoencephalitis." The results obtained corresponded to the experience of the research laboratory of the Children's Hospital in Philadelphia.

WALLGREN, Stockholm, Sweden.

MENINGOCOCCIC MENINGITIS: A FOLLOW-UP STUDY. W. J. GISELSSON, Nord. med. **38**:887 (April 30) 1948.

Of 40 patients having meningococcic meningitis before the introduction of sulfonamide treatment, 27 died and 2 were deaf-mutes. Of 34 patients treated with sulfonamide therapy or a combination of sulfonamides and penicillin, none died but three were deaf-mutes.

WALLGREN, Stockholm, Sweden.

EXTREME LEUCOCYTOSIS IN WHOOPING COUGH. JOHANNES THOMS, Nord. med. **42**:1233 (July 22) 1949.

Thoms reports a case of whooping cough in which the leucocyte count was 121,000 cells per cubic millimeter and there were 75% lymphocytes, most of which were immature.

WALLGREN, Stockholm, Sweden.

PENICILLIN TREATMENT OF SCARLET FEVER. HANS HELLSTEN and HANS STENQVIST, Nord. med. **42**:1475 (Nov. 9) 1949.

Six hundred patients with scarlet fever were treated with penicillin at Malmö Fever Hospital between Sept. 1, 1946, and Feb. 1, 1948. The last 400 patients received three doses daily and were isolated for nine to 10 days. Fourteen days later, before beginning school or work, the patients were subjected to control examination. The complications had been reduced to a minimum, consisting of transient synovitis (2.1%), tonsillitis (1.8%), otitis (0.33%), and cervical adenitis (0.33%).

WALLGREN, Stockholm, Sweden.

POSTVACCINAL ENCEPHALITIS. VAGN PETERSEN, Nord. med. **42**:1838 (Nov. 25) 1949.

Petersen reports the case of a 3½-year-old girl inoculated with smallpox vaccine 14 days before admission. A week later she fell ill with signs of encephalitis. The spinal fluid showed mild pleocytosis. The Pandy reaction was positive. The girl died 16 hours after admission. At the postmortem examination severe encephalomyelitis of the type seen in virus infections was found. The sister of the girl had measles four days before the girl fell ill. The author believes that there may be a connection between the measles and the vaccinia infection.

WALLGREN, Stockholm, Sweden.

DIPHTHERIA VACCINATION OF SCHOOL CHILDREN IN BERGEN. H. SCHNITLER and A. W. WORMNES, Nord. med. **43**:379 (March 3) 1950.

The authors report a follow-up study of children vaccinated with purified alum-precipitated diphtheria toxoid with two doses in 1942 and one additional dose in 1943. An investigation carried out six and one-half years after immunization proved that of 1,003 immunized school children 1,001 were Schick negative, and in the same series no diphtheria carriers could be detected.

WALLGREN, Stockholm, Sweden.

TREATMENT OF PERTUSSIS WITH HYPERIMMUNE SERUM. T. JOHNSSON and R. LUNDSTRÖM, Nord. med. **43**:784 (May 12) 1950.

Hyperimmune pertussis serum was given to 23 infants in the incubation period of whooping cough. Seventeen of the children were isolated from the source of infection during treatment. The treatment consisted in two injections with a six-day interval. In two of these 17 children a cough clinically not verified as whooping cough developed. The other 15 children remained free from the disease. Of the six children who were exposed to continued intimate contact with the source of infection, in five pertussis developed, four with a mild and one with a normal course. Hyperimmune serum could not prevent or make whooping cough milder in 30 children under the age of 2 yr. who were already in the whooping stage when treatment began.

WALLGREN, Stockholm, Sweden.

AUREOMYCIN TREATMENT IN COMPLICATIONS FOLLOWING SMALLPOX VACCINATION. B. APPELBOM and M. SCHNABEL, Nord. med. **44**:1790 (Nov. 10) 1950.

Four children, aged 2 to 8 years, with complications following vaccination (fever, secondary pustules, adenitis, conjunctivitis) were treated successfully with aureomycin. The possible effect upon the desired immunity in patients treated with aureomycin is discussed. The daily dose was 50 mg. per kilogram of body weight, with dosage continued for two to four days.

WALLGREN, Stockholm, Sweden.

THE IMMEDIATE PROGNOSIS IN POLIOMYELITIS. H. C. A. LASSEN and ERIK SKINHÖJ, Ugesk. læger **110**:905 (Aug. 8) 1948.

If the temperature remains above normal, it is probable that the paresis will continue to progress, though the chances of this being the case will be less from day to day. If the progression has stopped for 24 hours, the risk of further exacerbations diminishes considerably. An incipient fall of the temperature is not, however, in itself a prognostically good sign, as the development of paresis and the most pronounced progress of it most frequently occur during the lytic phase of the temperature curve. The degree of fever is without prognostic significance. When the temperature has once become normal, there is little risk of further progression of the disease.

WALLGREN, Stockholm, Sweden.

## Acute Infectious Diseases

THE EXPONENTIAL DEVELOPMENT OF PENICILLIN RESISTANCE BY NEISSERIA. FREDERICK MILLS, J. Infect. Dis. **85**:1 (July-Aug.) 1949.

The penicillin resistances of three strains of gonococci were increased about 20 to 70 times by passage through a series of tubes of broth with increasing concentrations of penicillin. Penicillin resistance of gonococci may be shown to plot exponentially against passages through penicillin medium. Further evidence is added by a statistical analysis.

Some adapted theories of Hinshelwood seem to indicate that development of penicillin resistance of Neisseria is due to the expansion of a single enzyme rather than replacement of a partially blocked enzyme by another. Only slight evidence was found for a relation between the individual resistant-rate coefficients, or slopes of the exponential curves.

TOOMEY, Cleveland.

STREPTOMYCIN STUDIES IN TULAREMIA: III. STREPTOMYCIN THERAPY IN MONKEYS. S. S. CHAPMAN, LEWIS L. CORIELL, and W. E. NELSON, J. Infect. Dis. **85**:45 (July-Aug.) 1949.

In five monkeys infected with Pasteurella tularensis the disease ran a fulminating course and terminated in death between the fourth and sixth days after infection. Five monkeys similarly infected were treated with streptomycin starting 48 hours after infection. The therapeutic effects were promptly manifested, and all treated animals survived. Two uninfected control animals which had received streptomycin showed no toxic effects which could be considered a contra-indication to the use of the drug. Clinical, laboratory, and pathological data on the course of tularemia in the monkey are presented.

TOOMEY, Cleveland.

GENERALIZED CYTOMEGALIC INCLUSION DISEASE. J. P. WYATT, J. SAXTON, and R. S. LEA, J. Pediat. **36**:271 (March) 1950.

Nuclear and cytoplasmic inclusion bodies have been found at autopsy in the salivary glands of from 10 to 32% of stillborn and live-born infants regardless of the cause of death. These inclusion bodies have been observed in other organs, largely in epithelial structures, such as bronchial epithelium, liver cells, and renal tubular epithelium, but have been regarded as an "incidental finding." The authors report six deaths in which these inclusion bodies were found at autopsy and appeared to have a significant part in the pathologic processes. They also have reviewed 60 similar cases from the literature. There is no typical clinical picture; the diagnosis has always been made at the autopsy table. The authors advance suggestive evidence that it is a viral disease.

MACDONALD, Pittsburgh.

FRIEDLÄNDER AEROGENES INFECTIONS IN INFANCY. W. OBRINSKY, R. DORMONT, and R. FOWLER, New Orleans M. & S. J. **103**:250 (Dec.) 1950.

Ten cases of Friedländer-aerogenes infection seen in one year are discussed. There were three patients with pneumonia, one with meningitis, one with genitourinary infection, and five with septicemia. All were infants. The three patients with pneumonia recovered, as did one of the patients with septicemia. Six patients died. Treatment consisted in administration of streptomycin, aureomycin, chloramphenicol, and sulfadiazine.

MCGUIGAN, Evanston, Ill.

ROCKY MOUNTAIN SPOTTED FEVER. L. J. RUTLEDGE, B. R. CLANTON, M. HOOD, and M. H. D. SMITH, New Orleans M. & S. J. **103**:261 (Dec.) 1950.

The authors described two cases of Rocky Mountain spotted fever occurring in Louisiana. Twenty previous cases had been reported in 10 years. Aureomycin or chloramphenicol are the drugs of choice. Sulfonamides should not be used.

MCGUIGAN, Evanston, Ill.

IMMUNOLOGIC AND BIOCHEMICAL STUDIES IN INFANTS AND CHILDREN WITH SPECIAL REFERENCE TO RHEUMATIC FEVER: VII. INHIBITION OF HYALURONIDASE BY SERA. NATHAN EPSTEIN, ROSE L. LUBSCHEZ, PAUL F. DE GARA, and MAY G. WILSON, Pediatrics **4**:569 (Nov.) 1949.

The serum inhibition of testicular hyaluronidase activity was determined by the turbidity method developed by Dorfman, with slight modifications. The serums studied were obtained from nonrheumatic and rheumatic children in apparent health and from rheumatic fever patients during active phases of the disease. The range in age was from 3 to 15 years. Results of the study can be summarized as follows: Human serum contains a heat-stable inhibitor of bovine hyaluronidase. No evidence was obtained that the serums of children susceptible to rheumatic

fever differed from those of nonsusceptible children in their capacity to inhibit bovine hyaluronidase activity. There was no significant difference in the degree of inhibition of hyaluronidase activity by serums of normal children, children with inactive rheumatic fever, and patients with rheumatic fever. After antecedent respiratory illness, presumably streptococcic in origin, maximum inhibition of hyaluronidase activity was observed for all three types of serum. There was no apparent relation between the phase of rheumatic fever, active or inactive, and the degree of inhibition of hyaluronidase activity. A small series of bovine serums failed to inhibit bovine enzyme. Two crude preparations of human hyaluronidase were not inhibited by human or bovine serums. The inhibition of bovine hyaluronidase by human serums may represent an immunologic reaction. No evidence was obtained to indicate that the inhibition to this enzyme system by serum from rheumatic patients is a reflection of the rheumatic process.

FROM THE AUTHORS' SUMMARY.

IMMUNOLOGIC AND BIOCHEMICAL STUDIES IN INFANTS AND CHILDREN WITH SPECIAL REFERENCE TO RHEUMATIC FEVER: VIII. RESPONSE TO PITUITARY ADRENOCORTICOTROPIC HORMONE (ACTH). KATHARINE HAIN and MAY G. WILSON, Pediatrics **4**:579 (Nov.) 1949.

This pilot study is concerned with a comparison of the adrenal cortical reserve in normal and susceptible children and in patients with active rheumatic fever, using the method described by Thorn and co-workers for determining the adrenal cortical reserve. Twenty-three children (8 girls, 15 boys) ranging in age from 6 to 13 years were observed. The corticotropin (ACTH) used in this study was given intramuscularly. No untoward reactions were observed in any of the 23 children tested. The following observations were made:

1. A single dose of 25 mg. of corticotropin administered intramuscularly to 23 children, including 9 nonrheumatic and 14 rheumatic children ranging in age from 6 to 13 years, was well tolerated. There was no significant difference in hematologic response in the groups studied. The uric acid/creatinine ratio was slightly higher in the rheumatic group.

2. The hematologic response four hours after corticotropin administration was characterized by a sharp fall of circulating eosinophiles ranging from —39 to —100%. The total rise in neutrophiles ranged from +5 to +67%. The differential smear showed a drop in lymphocytes from —19 to —55%.

3. The uric acid/creatinine ratio following corticotropin administration ranged from +113 to +105%.

4. The hematologic response to varied types of stress in eight children, including the response four hours after fasting, emotional stress, tonsillectomy, and insulin treatment, revealed a drop in circulating eosinophiles from —27 to —100% and a rise in leucocytes from 6,000 to 25,000 above prestress level.

5. The adrenocortical reserve as determined by the response to corticotropin was found to be within normal limits in the majority of rheumatic patients in this study.

It was concluded that the hematologic and metabolic effect of 25 mg. of corticotropin given intramuscularly did not appear to differ significantly among normal persons, susceptible persons, and patients with active rheumatic fever.

FROM THE AUTHORS' SUMMARY.

ACUTE DISSEMINATED HISTOPLASMOSIS IN CHILDREN: REPORT OF THREE CASES. JOHN H KNEIDEL and HAROLD SEGALL, Pediatrics **4**:596 (Nov.) 1949.

Three cases of proved histoplasmosis, two in infants and one in a child of 3 years, are presented. The mode of onset, clinical symptomatology, and laboratory and roentgenographic findings in these three cases are presented in detail.

All three cases terminated fatally, indicating that in the well-developed clinical case of histoplasmosis the prognosis appears hopeless. No effective fungicide is as yet available to combat this disease.

FROM THE AUTHORS' SUMMARY.

THRUSH IN INFANCY. H. LEDERER and R. McLAREN TODD, Arch. Dis. Childhood **24**:207 (Sept.) 1949.

In a series of 204 necropsies on infants under 12 months of age, 26 cases were encountered in which Candida albicans infection was responsible either directly or indirectly for the fatal

outcome. The danger of thrush infection to the infant, namely, extension into the esophagus with the subsequent syndrome of refusal of feeds, vomiting and dehydration, aspiration of vomit, septicemia, intestinal spread, and monilemia, is described. Diagnostic difficulties in the living and at necropsy may be responsible for a significant number of cases of fatal thrush lesions which remain undetected and unrecorded.

KELLY, Milwaukee.

ASCARIS IN THE COMMON BILE DUCT IN A CHILD. E. BLUM, R. SACREZ, and B. MONTRIEUL, Pédiatrie **37**:220 (March-April) 1948.

A 6-year-old child was admitted with complaints of violent cramp-like abdominal pains, which had existed in a milder form already for eight days. The temperature was elevated; there were no bowel movements for two days, and the child had been losing weight for the last three months. The abdomen was distended and extremely tender, particularly under the liver. In this region it was thought that a tumor could be found. There was no jaundice. Surgical exploration revealed a distended gall bladder with no foreign bodies. An incision in the common bile duct exposed a 20-cm.-long Ascaris. In the following days the patient passed a total of 43 roundworms. He made an uneventful recovery.

The authors discuss the differential diagnosis of the syndrome of abdominal pains, fever, and subhepatic swelling in a 6-year-old boy without obvious jaundice, including subhepatic appendicitis, cholecystitis, and cholelithiasis.

GLASER, Chicago.

BACILLUS PYOCYANEOUS INFECTION IN AN INFANT OF 5 MONTHS. R. TURPIN and M. BOUREL, Pédiatrie **37**:613 (Nov.-Dec.) 1948.

A 5½-month-old infant was admitted because of digestive and pulmonary disturbances and bilateral otitis media. Bilateral antrotomy was performed followed by drainage of blue pus from the mastoid regions and an abscess on the buttocks. This was followed by a bullous exanthema. Blood culture revealed Pseudomonas aeruginosa (Bacillus pyocyaneous). This infection responded to penicillin and sulfonamide therapy. The blood picture showed at first leucocytosis and slight anemia. The anemia became severe, and leukopenia developed.

The authors found in the literature only a few cases of Ps. aeruginosa infection reported and point out that whereas the clinical forms show a great variety the points of origin in infants are usually the umbilicus or the middle ear and mastoid region. This patient responded well to penicillin and sulfonamide therapy, but the authors feel that streptomycin may be the treatment of choice.

GLASER, Chicago.

THE DIAGNOSIS OF THE TYPHOID GROUP IN INFANCY. J. TAMÁSI and I. VINCE, Ann. pædiat. **176**:52 (Jan.) 1951.

The organism of the infant reacts differently from that of the adult, and its antibody production as compared with that of the adult is incomplete. Because of this, typhoid is clinically different in infants and in adults, and the test reactions also differ in the two age groups. In infants the clinical picture is not characteristic; the temperature curve is that of a septicemia. The most constant sign is the splenic tumor. The Widal reaction may be negative during the whole course of the illness. Positive agglutination never reaches high titer values, and the reaction is not constant. A positive agglutination in 1:100 dilution is suggestive, in 1:200 dilution indicative of typhoid. Positive culture in ox-bile is conclusive, but a negative culture does not exclude typhoid. Only frequently repeated examinations are of value. The same holds for the bacteriological examination of the stools. Seven cases of infantile typhoid are discussed: Two were caused by Salmonella typhosa, five by S. paratyphi B. In three cases the diagnosis was decided by a positive ox-bile culture; in one of these cases the Widal reaction was negative, in the two others the agglutination titer was fairly high. In four other cases the diagnosis was made only on the basis of the agglutination reaction. All the infants recovered.

FROM THE AUTHORS' SUMMARY.

TACHYCARDIA IN PERTUSSIS. G. FANCONI and W. FRISCHKNECHT, Helvet. paediat. acta **5**:113 (May) 1950.

Sinus tachycardia of long duration in cases of pertussis was found to have a cerebral or cardiac origin. In two cases reported, the electrocardiogram may represent reversible changes.

Cardiovascular decompensation in cases of pertussis (with reversible changes of the electrocardiogram) occurs with or without sinus tachycardia.

In a series of 220 infants and children with pertussis, only two had signs of cardiovascular decompensation. Six infants with marked cerebral involvement showed tachycardia without any signs of cardiac disease.

FROM THE AUTHORS' SUMMARY.

FIRST RESULTS FROM CHLOROMYCETIN TREATMENT OF TYPHOID IN CHILDREN. MARIO VERROTI, Clin. pediat. **32**:61 (Feb.) 1950.

The author, after a brief description of the antibiotic properties of chloramphenicol (chloromycetin®), describes five infants with typhoid, some very seriously ill, treated with this antibiotic. He concludes with some clinical and therapeutic considerations.

FROM THE AUTHOR'S SUMMARY.

FREQUENCY OF HEMOAGGLUTINATION FROM COLD IN SOME VIRUS DISEASES OF CHILDREN. C. STICCA, Minerva pediat. **2**:465 (Oct.) 1950.

The titer of cold agglutinins in uncomplicated virus pneumonia will not be under 1:64 or over 1:128, a finding which is important in the differential diagnosis.

The titer in 75 children with other virus infections (measles, roseola, varicella, poliomyelitis, parotitis, scarlet fever) was never in excess of 1:32, except when there was pulmonary disease.

HIGGINS, Boston.

ACTION OF DESOXYCORTICOSTERONE ACETATE ON THE BIOCHEMISTRY OF THE BLOOD IN SOME INFECTIOUS DISEASES. F. MULÈ, P. SEDATI, and L. GERUFI, Pediatria **58**:153 (March) 1950.

The colloid dispersion, the sedimentation rate, and the glutathione content of the blood were determined in cases of measles, scarlet fever, and typhoid before and after the injection of desoxycorticosterone acetate. The blood colloid relations tended to return to normal after the injections and were associated with an increase in the glutathionemia.

HIGGINS, Boston.

WATERHOUSE-FRIDERICHSEN SYNDROME. LUIS CARDONA MATEO, Acta pediat. españ. **88**:421 (April) 1950.

Mateo presents a case of Waterhouse-Friderichsen syndrome in a 3-year-old girl who died less than 20 hours after onset. He reviews the literature and history of the disease. Mateo believes many cases go undiagnosed and unreported.

The symptoms are of three types: (1) those due to and indicative of an infection, such as fever, vomiting, headache, psychomotor excitement, and sometimes convulsions; (2) those due to circulatory collapse, such as cyanosis, especially of extremities, filiform pulse, low blood pressure, tachycardia, dyspnea, and the marble-like appearance of extremities and ears; (3) hemorrhages into the skin, either petechial or diffuse; they may be true hemorrhages or minute emboli. Meningeal symptoms may or may not be present.

The positive laboratory findings are leucocytosis, granulocytosis, and immature forms, both red and white. The platelet count is normal, as are the bleeding and coagulation times. Blood cultures may show organisms, most commonly the Meningococcus. Blood sugar is low, and total nitrogen is elevated, as is the blood urea.

The anatomical findings are massive hemorrhage, which is nearly always bilateral, into the adrenal glands. Hemorrhages may be petechial or massive in other organs, such as the lungs, the gastrointestinal tract, and serous and mucous membranes. The thymus gland is usually enlarged. The same hypertrophy is noted in the other lymphatic tissues, especially the tonsils and pharyngeal lymphatic nodes.

The etiological factors are age and constitution. Most cases occur in infants but cases may occur even in adults. According to Aegerter, 70% of all patients are between 2 months and 2 years of age. Kamber reported a study of 61 cases and found 40% of the patients under 2 years of age.

Some investigators point to the soft pasty appearance of tissues in the children affected; others point out the lymphadenitis, frequently considered as a meningococcic septicemia, although

other organisms, such as Pneumococcus, Streptococcus, and Hemophilus influenzae, have been isolated in blood cultures. There has been much discussion about which is primary—the infection or the adrenal symptoms; some believe the organisms have a tropism for adrenals, while some have suggested an anaphylactic origin, with the infection only incidental.

Dr. Perez Soler believes that the syndrome is nothing more than very severe infection in an infant with a background or constitution of vagosympathetic dysfunction. Meneghello believes there is some significance to the adrenal symptoms but they are difficult of interpretation because of the additional factors of overactivity of the lymphatics and insufficiency of the adrenals.

The author then lists the conditions which must be differentiated from this syndrome: 1. respiratory infections; 2. circulatory diseases; 3. status thymolymphaticus; 4. acute abdominal diseases; 5. severe toxic states; 6. blood dycrasias, especially (*a*) fulminating Henoch's purpura and (*b*) acute essential thrombopenia; 7. fulminating respiratory infections.

Mateo says that although the disease is almost always fatal, treatment should be initiated early and medication should be massive and directed at the infection and the impending suprarenal and circulatory collapse.

Sulfonamides and penicillin in massive doses and heart stimulants, such as epinephrine pentylenetetrazol, ephedrine, and nikethamide, and extracts of adrenal cortex should be tried. Isotonic sodium chloride solution and dextrose, blood transfusions and plasma administered intravenously should be used also.

ALLEN, Santa Fe, N. M.

LYMPHATIC AMEBIASIS IN 5-YEAR-OLD CHILD. FLORENCIO BAZAN and ENRIQUE SUJOY, Arch. argent. pediat. **30**:314 (Nov.) 1948.

Bazan and Sujoy review the literature of lymphoglandular amebiasis and describe what they believe to be the first case of the disease reported in a child. After a four-month illness characterized by fever, abdominal pain, diarrhea, loss of weight, languor, and extreme pallor, the child showed greatly enlarged, tender, and fluctuant lymph nodes of the inguinal region. At the same time, a tender mass was palpated deep in the right iliac fossa and was assumed to be iliac lymphadenopathy. Aspiration of one of the inguinal nodes revealed large numbers of both cystic and trophozoitic amebas. Stool examinations were likewise positive for both forms. Treatment consisted of emetine, 0.02 gm. daily, subcutaneously, and amebarsone, 0.3 gm. daily for 10 days, resulting in remarkable general improvement and disappearance of both inguinal and iliac masses. A second series of treatments was delayed, with recurrence of intestinal findings but not of the lymphadenopathy. Retreatment resulted in complete clinical cure.

PANOS, Galveston, Texas.

HEMORRHAGIC INFARCTION OF THE TESTICLE. SEBASTIAN A. ROSASCO, Arch. argent. pediat. **32**:382 (Nov.) 1949.

Two cases of testicular infarction in the newborn are presented, with reference to a general discussion of etiology and classification.

PANOS, Galveston, Texas.

VASCULAR CHANGES IN LOWER EXTREMITIES IN 13-MONTH-OLD INFANT AS FIRST MANIFESTATION OF ESCHERICHIA COLI SEPTICEMIA: CURE WITH STREPTOMYCIN. V. O. VISILLAC, T. M. BANZAS, and J. M. OLIVE, Arch. argent. pediat. **30**:277 (Dec.) 1948.

The following signs of acute vascular occlusion in both lower legs appeared suddenly in an apparently well infant: intense pain, cyanosis, cold skin. The wine-red cyanotic areas soon became well demarcated, and numerous vesicular and necrotic lesions appeared, especially on the right leg. The right dorsalis pedis artery could not be palpated because of the lesions; the left was normally palpable. By the third day, the clinical condition became critical, with high fever, prostration, peripheral vascular collapse, splenomegaly, and a generalized "rose-spot" rash. The following day, blood culture grew out Escherichia coli, and therapy with streptomycin was begun. Soon thereafter, signs of left orchitis and epididymitis also appeared. Blood culture was negative for escherichiae after 48 hours. Improvement in all aspects was quite rapid and proceeded to full recovery within 15 days.

The differential diagnosis is discussed, and the authors conclude that the E. coli bacteremia resulted in embolic occlusion of the "arteriolocapillary system" in both lower legs. There was no identified focus of infection.

PANOS, Galveston, Texas.

TREATMENT OF TOXIC AND MALIGNANT DIPHTHERIA WITH ADRENAL CORTEX HORMONE. JOERN GLEISS and HEINZ NIGGEMEYER, Arch. Kinderh. **137**:168 (Sept.) 1949.

The experience of the authors is based on the treatment of 299 children, 2 to 13 years of age, with various preparations of adrenal cortex extracts for malignant, severe, and medium severe diphtheria in the University Children's Hospitals of Hamburg and Düsseldorf. Application of adrenal cortex extracts had no effect when the heart muscle was already damaged. When these was given very early, the initial circulatory collapse was influenced favorably.

The final fatal outcome of diphtheria may be delayed but cannot be prevented, as is shown from the mortality rates. The tendency to hemorrhages is definitely reduced by adrenal cortex extracts. The authors recommend careful dosage of the extracts and they emphasize the danger from overdosage, especially of anuria.

ARON, Chicago.

REINFORCED TREATMENT OF PERTUSSIS. WILHELM HERTZ, Arch. Kinderh. **137**:73 (Aug.) 1949.

Of a total of 160 children with pertussis, 38 were treated for two weeks with injections of pertussis vaccine simultaneously with injections of 1.0 to 3.0 cc. of sterilized milk. After initial bouts of fever and an increased number of coughing spells for a few days, these children showed favorable results under this treatment as compared to those who were given pertussis vaccine only.

ARON, Chicago.

## Diseases of Blood, Heart, and Blood Vessels and Spleen

PERSISTENT PATENT DUCTUS ARTERIOSUS. RALPH BOERNE BETTMAN, Illinois M. J. **97**:87 (Feb.) 1950.

A persistent patent ductus arteriosus is a pathological condition which may be harmful either because of the change in the mechanics of the circulation or because of the increased tendency toward subacute bacterial endarteritis.

The symptoms subsequent to the altered mechanics simulate those of cardiac insufficiency or other conditions which produce fatigue or malnutrition. The signs are strikingly evident. They consist of a loud, easily audible, continuous murmur best heard over the second left interspace, and an easily palpable thrill over the entire precordium; these two signs along with the absence of cyanosis should make any physician suspect the presence of an aortic-pulmonary artery shunt. Ligation or suture of the patent ductus cures the condition. The operation, especially in the absence of a complicating endarteritis, is simple, and the risk involved minimal in comparison with the danger of the disease and in view of the excellent results obtained.

FROM THE AUTHOR'S SUMMARY.

ANGIOCARDIOGRAPHY IN INFANTS AND CHILDREN: NEW TECHNIC. JOHN D. KEITH and JOHN D. MUNN, Pediatrics **6**:20 (July) 1950.

An apparatus is described which permits taking four roentgenograms a second. Its use in angiocardiography is demonstrated by a series of cases of congenital cardiac anomalies. This method of investigation has proved most useful in studying the cyanotic group and in demonstrating shunts from right to left. A variety of different technics may, however, yield useful information in the noncyanotic group also. The procedures outlined are most valuable in the newborn period, where congenital cardiac anomalies are commonly encountered and where their differentiation is particularly difficult. The information collected in this manner has been, in many instances, a help to the surgeons in planning suitable surgery.

FROM THE AUTHORS' SUMMARY.

DETERMINATION OF OXYGEN CONTENT OF CAPILLARY BLOOD IN CONGENITAL HEART DISEASE. HERBERT N. HULTGREN and ADELINE J. HACKETT, Pediatrics **6**:93 (July) 1950.

A previously described technique of collecting and analyzing capillary blood for oxygen content has been modified slightly and applied in the study of children with congenital heart disease. Samples obtained and analyzed in this manner differed in oxygen content from simultaneously drawn arterial samples by no more than 0.4 vol. %. The value of the technique in the study of congenital heart disease has been illustrated.

FROM THE AUTHORS' SUMMARY.

RECENT ASPECTS OF CONGENITAL HEART DISEASE. M. IBRAHIM, A. EL SHERIF, A. SOROUR, and M. ATTIAH, J. Roy. Egyptian M. A. **32**:741 (Oct.) 1949.

Newer methods of diagnosis in congenital heart disease are discussed, including cardiac catheterization and angiocardiography. Treatment by surgery is mentioned very briefly.

McGUIGAN, Evanston, Ill.

ON THE EFFECT OF SECONDARY INFECTIONS ON THE DEVELOPMENT OF HOOKWORM ANEMIA: OBSERVATIONS ON THE ROLE OF SECONDARY INFECTIONS IN IRON DEFICIENCY ANEMIA. EUGENE STRANSKY and DOMICIANA DAUIS-LAWAS, Ann. pædiat. **173**:281 (Nov.) 1949.

The response of hookworm anemia in children suffering from different intercurrent diseases, such as chronic nephritis, tuberculosis, rheumatic heart disease, congenital malformation of the heart, infectious hepatitis, amebic dysentery, and liver cirrhosis due to Schistosoma japonicum infestation, to iron treatment was studied. In chronic nephritis there is no improvement of the anemia, owing to the toxic depression of the bone marrow activity leading to anemia even without hookworm anemia. In all other conditions if the process is not too advanced, the improvement has been similar to improvement observed without any secondary disease. As hookworm anemia is clear-cut iron-deficiency anemia, we have to revise our opinion on the behavior of iron-deficiency anemias beyond infancy in case of secondary or intercurrent diseases as well as infections.

FROM THE AUTHORS' SUMMARY.

ACUTE HEMOLYTIC ANEMIA AFTER INGESTION OF BEANS (FABA VULGARIS) AND ITS TREATMENT. BAHTIYAR DEMIRAG, Ann. pædiat. **173**:314 (Nov.) 1949.

A description is given of three cases of severe hemolytic anemia after the ingestion of raw or cooked beans (Faba vulgaris). The toxic symptoms were observed in children who never before had been in contact with this food, but also they were seen in children who had eaten the same kind of beans previously without exhibiting any signs of idiosyncrasy.

As the consumption of these beans is widespread, but toxic symptoms are but rarely observed, it has to be assumed that a constitutional disposition is necessary to produce this specific idiosyncrasy and intoxication.

One of the cases became complicated by a fresh infection with Plasmodium vivax, transmitted by blood transfusion, which had become necessary to combat the severe anemia. When the initial hemolytic anemia caused by the intoxication improved, the malaria infection was responsible for a second phase of hemolytic anemia which had, however, a much milder course and was cured with quinacrine hydrochloride (atabrine) therapy.

Besides blood transfusion, intramuscular injection of 0.5 cc. a day of 4% cholesterol in oil proved of value to combat the acute hemolysis.

FROM THE AUTHOR'S SUMMARY.

STUDY OF ALL CYANOTIC CONGENITAL CARDIOPATHIES OBSERVED IN ZURICH CHILDREN'S HOSPITAL AND DIFFICULTIES OF DIAGNOSIS. E. ROSSI, M. GROB, and M. BETTEX, Helvet. paediat. acta **5** (Supp. to No. 4):49 (July) 1950.

A review of the cases of congenital cardiac defects with cyanosis observed at the Children's Hospital in Zurich, in which the modern clinical techniques for diagnosis were used, is in close agreement with the symptomatology known from previous reports in the literature. Some details, for example, the changes of the mucous membranes and the capillaries, as well as the

relation of heart configuration to the body form, are especially stressed. Differential diagnosis of various forms of cyanotic heart failure is discussed. While the differentiation of the tetralogy of Fallot and the Eisenmenger complex is easily made in typical cases, dilatation of the pulmonary artery requires an especially thorough examination. The absence of roentgenologically visible congestion of the lungs led to a false diagnosis of tetralogy of Fallot in a case of Eisenmenger complex. In the differential diagnosis between tetralogy of Fallot and pseudotruncus arteriosus, angiocardiography in the anterior oblique diameter is very important.

Differentiation of Fallot's tetralogy from pulmonary stenosis with a defect of the interauricular septum is extremely difficult, as the physiopathologic conditions are essentially the same. Special roentgenologic findings and determination of oxygen saturation may help in making the diagnosis. As shown in one case, angiocardiography may lead to misinterpretation.

Transposition of the great vessels and atresia of the tricuspidalis present less diagnostic difficulty. Disturbances in the torsion of the heart *in toto* (mesocardia and dextrocardia) and their combination with Fallot's tetralogy are briefly mentioned.

Owing to modern procedures of examination, it is usually possible to overcome most diagnostic difficulties. It may be the angiocardiography, the measuring of intracardial pressure, or the determination of the oxygen saturation which will help the right diagnosis to be made. In many cases, however, only the results of all examinations may lead to a diagnosis. None of the procedures, therefore, should be neglected. The omission of one test may lead to diagnostic errors and have disagreeable consequences in surgical treatment.

FROM THE AUTHORS' SUMMARY.

"LEUKEMOID EOSINOPHILIA." H. MORF, Helvet. paediat. acta **5**:505, 1950.

Five cases with marked leucocytosis and high eosinophile counts are described. The increase of eosinophiles lasted for months and partly for years. There were also swellings of the liver, spleen, and lymph nodes and in some cases transitory infiltrations of the lung and urticaria. The described cases are classified as "eosinophilic leukemoids."

As etiological factors were found in three cases ascariasis, in one familial case an infection of Fasciola hepatica. In another case a disturbance in milk absorption combined with an infection was suspected. The striking fact that in three cases other members of the family showed increased eosinophiles as well seems to prove a constitutional disposition for eosinophilia.

FROM THE AUTHOR'S SUMMARY.

MARKED EOSINOPHILIA IN A CHILD. INGER HÖJER, Nord. med. **41**:466 (March 11) 1949.

Höjer reports the case of a 20-month-old boy who had been well until three months before admission, when he became fretful, cried, and lost his appetite and vomited. At the examination liver and spleen were found moderately enlarged. Peripheral lymph nodes were slightly enlarged. Internal organs were otherwise without abnormality. The hemoglobin level was 59%, erythrocytes 4,670,000, and leucocytes 33,200, with polymorphonuclear leucocytes 8%, eosinophiles 67%, small lymphocytes 14%, large lymphocytes 9%, and monocytes 2%. Bone marrow showed normal conditions apart from considerable infiltration of eosinophiles, 12% mature and 12% immature. There were no parasites in the stools and no blood. Skin tests with different allergens showed nothing abnormal. He was treated with iron and vitamin D. His general condition greatly improved, and the blood became normal. At his discharge the eosinophiles were 22%, total leucocytes 12,200. The author believes the eosinophilia to be due to some allergic factor that could not be demonstrated.

WALLGREN, Stockholm, Sweden.

ACUTE HEMOLYTIC ANEMIA (LEDERER TYPE). BJARNE MERRILD-HANSEN, Nord. med. **42**:1641 (Oct. 14) 1949.

A 12-year-old girl who had suffered from diarrhea for two weeks previously fell ill one week later with jaundice, with dark-colored urine, high fever, severe anemia (hemoglobin 11%, red blood cells 910,000, leucocytes 16,000), and urobilinuria. Bone-marrow puncture showed anemia of simple type in regeneration. Osmotic resistance of the red blood cells was normal.

Reticulocytes at the admission were 14.9%, the sedimentation rate 156 mm. After blood transfusion rapid recovery occurred. The patient was discharged as healthy after three weeks of hospitalization. Follow-up examinations two and six weeks later showed a normal condition.

WALLGREN, Stockholm, Sweden.

LEUKEMIC RENAL TUMOR AND UREMIA. J. R. MYHRE, Nord. med. **43**:75 (Jan. 13) 1950.

A 13-year-old boy fell ill with signs of uremia, hypertonia, and albuminuria. At admission the blood picture was normal. Three weeks later the white-blood-cell count was of the leukemic type. In the meantime the general condition of the boy had deteriorated; he displayed edema and high blood-urea clearance, and bone marrow puncture showed almost only pathological cells. He died after one month's illness. Both kidneys were palpable through the abdomen. At post-mortem examination the kidneys were found to be enlarged, 380 and 350 gm., pale, with homogeneous cut surface; microscopic examination showed leukemic infiltrations.

WALLGREN, Stockholm, Sweden.

SPLENECTOMY IN A CASE OF HEMOPHILIA WITH TRAUMATIC RUPTURE OF THE SPLEEN, ACCOMPANIED WITH DIMINISHED DISPOSITION TO HEMORRHAGE. AUG. FABRIN LUND, Nord. med. **43**:631 (April 14) 1950.

A 10-year-old hemophilic boy had a traumatic rupture of the spleen with recovery after splenectomy. The disposition to hemorrhage seemed to have diminished after operation, but the clotting time was still protracted.

WALLGREN, Stockholm, Sweden.

PHLEBOSTENOSIS SPLENICA (SPLENOPORTAL STENOSIS) IN CHILDREN. L. H. GABRIELSEN, Nord. med. **44**:1638 (Oct. 13) 1950.

Gabrielsen reports six cases of children aged 2 to 11 years with phlebostenosis. Three children suffered from recurrent bleedings, and two of these died. In four cases the disease was believed to be due to umbilical infections during early infancy. No alterations of the veins could be found in the five patients operated upon (splenectomy), while autopsy revealed such changes in two cases. No evidence of liver damage could be demonstrated in any of these patients. One child is still living, to all appearance in good health two years after operation.

WALLGREN, Stockholm, Sweden.

PERIARTERITIS NODOSA, LEUKEMOID REACTION, AND EXCESSIVELY INCREASED ANTISTREPTOLYSIN TITER. BERTEL VON BONSDORF, Nord. med. **44**:1874 (Nov. 24) 1950.

The case of a 9-year-old girl is reported. The most prominent manifestations were remittent fever, subcutaneous infiltrations and nodules, ankylotic inflammation of the joints, muscular atrophy, abdominal pain, and hematuria. The disease was self-limited and the recovery complete, but relapses occurred. The blood showed a leukemoid reaction, highest leucocyte count 142,400, with myelocytes. The antistreptolysin titer was markedly increased, with the highest value 6,400. The author considers the last sign a token of a relation between periarteritis nodosa and rheumatic fever.

WALLGREN, Stockholm, Sweden.

HISTIOCYTOSIS. J. ISINGRUD, Nord. med. **44**:1876 (Nov. 24) 1950.

Isingrud reports a case of histiocytosis in a boy 1½ years old. The disease started with otorrhea, for which operation was done. Later severe anemia and enlargement of the liver and spleen occurred, as well as hemorrhages in the skin. The boy died at the age of 2 years, from what seemed to be a septic disease, having been ill for nine months. At autopsy multiple areas of destruction were found in the skull and the temporal bone, as well as foci in the internal organs with a histologic picture of Letterer-Siwe disease (transformation into Schüller-Christian disease?).

WALLGREN, Stockholm, Sweden.

SPORADIC HEMOPHILIA. HOLGER DYGGVE, Ugesk. læger **110**:527 (April 29) 1948.

The author reports two cases of hemophilia, the patients two boys, aged 1 and 2 years, with the usual signs and symptoms. There were no other known cases in the families or in ancestors. The mothers of these two children had, however, a markedly increased clotting time. It is maintained that there is no difference between sporadic and ordinary hereditary hemophilia.

WALLGREN, Stockholm, Sweden.

MEGALOCYTIC ANEMIA IN A 19-MONTH-OLD INFANT. P. H. D. WAAGSTEIN, Ugesk. læger **110**:1150 (Oct. 7) 1948.

A male breast-fed infant of 19 months was admitted with the tentative diagnosis of anemia gravis (acute leukemia). The parents and a 7-year-old brother were healthy. The child had normal development and had been quite healthy until 11 months of age, when he had acute pneumonia. At the same time intestinal troubles, consisting of diarrhea alternating with constipation, started and were unsuccessfully treated by diet. Eventually he became anemic. At examination the hemoglobin level was 30%, red blood cells 910,000, color index 1.45, leucocytes 7,640 per cubic millimeter with lymphocytosis, reticulocytes 40 per thousand. There were numerous megaloblasts and megalocytes. Bone marrow study showed hyperplastic, megaloblastic anemia. Hydrochloric acid was present in the gastric juice. Spleen and liver were without change. Rapid improvement and normalization of the blood were brought about by administration of liver preparations, vitamin B, and iron. After the liver treatment had been stopped, a relapse set in, with satisfactory response to new liver therapy. WALLGREN, Stockholm, Sweden.

TRANSPOSITION OF THE GREAT VESSELS. J. H. P. JONXIS and P. J. KOOREMAN, Maandschr. Kindergeneesk. **17**:136, 1949.

A description is given of two cases of transposition of the great vessels. The first patient died at 8 months of age. At autopsy the ventricular septum was intact, but there was a defect of the atrial septum. The second patient, a boy of 11 years, showed the syndrome of Taussig: transposition of the great vessels and a high ventricular septal defect and a dilated pulmonary artery. Especial attention is given to the problem of oxygen tension in the tissues.

FROM THE AUTHORS' SUMMARY.

INDICATIONS FOR SPLENECTOMY IN CASES OF THROMBOPENIA IN CHILDREN. T. D. STAHLIE, Maandschr. Kindergeneesk. **18**:64, 1950.

After having discussed the pathogenesis of thrombopenic purpura, the writer arrives at the following conclusions:

1. Splenectomy is very rarely indicated in children, as the disease shows tendency toward spontaneous cure even after a long time (over two years).

2. If, on account of the chronicity and/or severity of the symptoms, splenectomy has to be seriously considered, it is strongly advised to ascertain first whether the megakaryocytes of the bone marrow show a "maturation arrest" or not; in cases of simple hypoplasia of the megakaryocytes, splenectomy should not be performed.

Seven illustrative case histories are given.

FROM THE AUTHOR'S SUMMARY.

## Diseases of Nose, Throat, and Ear

THE REHABILITATION OF THE STUTTERER. WENDELL JOHNSON, Illinois M. J. **98**:341 (Dec.) 1950.

Johnson points out that there is marked variation in the stutterer's performance. No adequate estimates of vocational disadvantage have been made, but general knowledge indicates that the handicap probably amounts to an average of roughly 25% at least in earning power. Clinical and test studies of personality have shown that, as a group, stutterers come close to approximating general population norms. Their special areas of maladjustment center around

the anxiety reactions they tend to make to the embarrassing and handicapping frustrations arising out of their stuttering. Personal and social maladjustments, due to this or other factors, tend, when present, to aggravate the speech difficulty.

Regarding etiology, currently the theory that stuttering is a learned form of hypertonic avoidant behavior, motivated by anxiety concerning the anticipated occurrence of nonfluency and its social consequences, appears to be receiving particularly serious consideration by the majority of speech pathologists.

Details of present methods in examination and diagnosis are discussed. In treatment, very young stutterers are nearly always best treated indirectly by means of properly detailed counseling of the parents. Direct treatment divides generally into psychological counseling and directed changes in habitual speech performance. Properly instructed, most stutterers can learn to do their stuttering more simply, with decreased tension and less emotional disturbance. The author lists several ways in which improvement is to be gauged. Professional qualifications essential for clinical work with stutterers are defined by the American Speech and Hearing Association. The treatment of stuttering consists in a program requiring teamwork among all those who influence the stutterer's speech adjustments.

BARBOUR, Peoria, Ill.

ACUTE LARYNGO-TRACHEO-BRONCHITIS AND ITS MANAGEMENT. HANS VON LEDEN, Illinois M. J. **99**:10 (Jan.) 1951.

During the year 1949, there were 70 patients with acute laryngotracheobronchitis seen at St. Francis Hospital, Evanston, Ill., of a total of 2,060 admissions to the pediatric department. This represents more than 3% of the total admissions. Eighty per cent of the tracheotomized patients were boys. The patients ranged in age from a few months to 14 years, although the ages of 1 to 3 are the commoner ones.

According to Von Leden, results obtained in the treatment of acute laryngotracheobronchitis depend directly on a thorough understanding of the underlying physiologic and pathologic processes and an application of these principles to the management. Early recognition and hospitalization, good medical supportive care, including the use of a heatless humidity unit, and prompt tracheotomy when surgical intervention is indicated lead to a better prognosis and decrease the mortality for this disease. Eleven consecutive patients with acute, fulminating laryngotracheobronchitis treated by tracheotomy without a mortality prove the value of this management.

BARBOUR, Peoria, Ill.

TECHNIQUES OF THERAPY FOR PRE-SCHOOL CHILDREN. JANE BEASLEY, J. Speech & Hearing Disorders **14**:307 (Dec.) 1949.

A combination of group and individual instruction two hours a day for a period of two weeks was carried out for four such two-week periods and a total of 16 preschool children. The following conclusions were made: 1. Direct study of a child's behavior in interpersonal relations with his peers provides more adequate information on which to base both clinical and home procedures. 2. Direct clinical training can establish a broad base of experience-participation in group activity on which to base both clinical and home procedures. 3. Direct clinical training for children enables parents to gain better understanding of their children and more insight in how to give effective assistance to the child at home.

PALMER, Wichita, Kan.

DIADOCHOKINETIC MOVEMENTS OF NINE-, TEN-, AND ELEVEN-YEAR-OLD CHILDREN. BETTY L. BLOOMQUIST, J. Speech & Hearing Disorders **15**:159 (June) 1950.

A group of 60 white children (10 girls aged 9 years, 10 boys aged 9 years, 10 girls aged 10 years, 10 boys aged 10 years, 10 girls aged 11 years, and 10 boys aged 11 years) were taken in groups and instructed to repeat, as rapidly and as regularly as possible, the following: "p, p, p; t, t, t; k, k, k; ptk, ptk, ptk." They then repeated the series twice again. The results were as follows: The number of sounds produced each second increased with age for each of the sounds tested. Boys made slightly higher scores than girls in the same age group for all sounds except the serial repetition of "ptk." None of the differences were significant. Further study is indicated.

PALMER, Wichita, Kan.

TYPE OF BIRTH AS RELATED TO STUTTERING. JOHN L. BOLAND JR., J. Speech & Hearing Disorders **16**:40 (March) 1951.

Two hundred nine stutterers with a sex ratio of approximately four boys to one girl were studied for the occurrence of instrumental delivery among the group. The percentage of instrumental delivery was compared with available records from various hospitals and other surveys. The results of the study indicate that instrumental birth and stuttering may be positively related.

PALMER, Wichita, Kan.

CHIPPED GLASS AS A PROBABLE CAUSE OF RETROPHARYNGEAL ABSCESS IN AN INFANT. LYTT I. GARDNER and HORST J. HEINICKE, New England J. Med. **242**:975 (June 22) 1950.

A 10-month-old girl entered Massachusetts General Hospital because of hemoptysis and a swelling in the neck. Two days prior a chip of glass was found to be missing from a baby-soup jar from which the child had been fed. The first bloody vomitus had appeared during a feeding from this jar.

Dysphagia, respiratory obstruction, and high fever marked the course of the illness, but a favorable outcome was gained by virtue of two operative decompressions, chemotherapy, and parenteral alimentation, although the chip was never found. This is the fourth case report involving glass baby-food containers, and the prevention of such accidents is discussed.

WHEELOCK, Denver.

FAMILIAL CONGENITAL STRIDOR. HARRY V. L. FINLAY, Arch. Dis. Childhood **24**:223 (Sept.) 1949.

Reference is made to the more important papers illustrating the development of our present knowledge of laryngeal stridor in early infancy. The clinical notes and postmortem findings of three children in one family, all showing congenital stridor, are presented. The last patient was shown to have an abnormal origin and course of the right subclavian artery. Two of the children died shortly after laryngoscopy.

KELLY, Milwaukee.

ANESTHESIA FOR TONSILLECTOMY AND ADENOIDECTOMY. H. M. SLATER and C. R. STEPHEN, Canad. M. A. J. **64**:22 (Jan.) 1951.

The authors point out the need for careful anesthesia in tonsillectomy. Attention is called to proper premedication and induction to avoid psychic trauma. Ideal anesthesia requires the use of an endotracheal tube. The safest anesthetic agents are a combination of nitrous oxide, oxygen, and ether. Careful watch must be kept for the development of anesthetic complications during and after operation.

MCGUIGAN, Evanston, Ill.

MAXILLARY SINUSITIS IN CHILDREN—A TREATMENT TECHNIQUE. R. H. VON DER BORCH, Clin. Rep. Adelaide Child. Hosp. **1**:216 (May) 1949.

The author describes his method of treating maxillary sinusitis by lavage through indwelling tubes in the antrums.

MCGUIGAN, Evanston, Ill.

CASE OF PHARYNGITIS FROM THE ENTEROCOCCIC STAPHYLOCOCCUS. P. TOLENTINO and R. M. RAVASI, Minerva pediat. **2**:172 (April) 1950.

A 2-year-old child had diarrhea shortly after acute pharyngitis. Culture of throat swabbings revealed the presence of an enterotoxic Staphylococcus.

HIGGINS, Boston.

IMPAIRMENT OF HEARING IN SCHOOL CHILDREN AND ITS CAUSES. NILS LUNDGREN, Nord. med. **38**:1015 (May 21) 1948.

Among 1.426 Swedish school children examined audiometrically, impairment of hearing for high tones was found in 9.1% and impairment for all tones in 5.1%. None of the former impairments and only 3.1% of the latter were discovered with ordinary whispering test. Only

0.35% had a loss of hearing great enough to be a serious disadvantage. Twenty per cent of the children had suffered from otitis media. Chronic otitis media was present in 13 patients, three of whom had had cholesteatoma and had been subjected to radical mastoidectomy. In 31.3% of the children adenoidectomy had been performed without any evident influence on the hearing.

WALLGREN, Stockholm, Sweden.

CHLOROMYCETIN IN PSEUDOCROUP. BERTIL SÖDERLING, Nord. med. **44**:1180 (July 21) 1950.

Twenty-five children below 2 years of age with moderately severe or severe pseudocroup were treated with chloramphenicol (chloromycetin®), 50 to 100 mg. per kilogram of body weight daily, divided in four to six doses, for two to three days. In most cases a good effect was achieved after only five to six hours. Treatment for two days, in exceptional cases three days, is recommended. There were no untoward effects.

WALLGREN, Stockholm, Sweden.

FOLLOW-UP STUDY OF TONSILLECTOMIZED CHILDREN. PER PERMIN, Nord. med. **44**:1728 (Oct. 27) 1950.

Sixty-seven children tonsillectomized or tonsillotomized were examined five to 20 years later; 85% of the patients presented postoperative improvement.

WALLGREN, Stockholm, Sweden.

## Diseases of the Lungs, Pleura, and Mediastinum

ORGANOID DIFFERENTIATION OF THE FETAL LUNG: A HISTOLOGIC STUDY OF THE DIFFERENTIATION OF MAMMALIAN FETAL LUNG IN UTERO AND IN TRANSPLANTS. WILLIAM W. WADDELL, Arch. Path. **47**:227 (March) 1949.

The author in this article investigates the genesis of mammalian pulmonary tissue. He studied uninterrupted serial sections of tissues from the fetal lungs of the mouse, guinea pig, and human being at different ages of gestation. Another method he employed utilized the techniques of transplanting fetal lung tissues into the anterior chamber of the eyes of guinea pigs and into the subcutaneous tissues of homologous adults. For these he used tissues from the mouse, guinea pig, and rabbit. Fetuses in the first trimester were found better suited for study of the developing bronchi, those in the second and third trimesters better for investigation of alveolar differentiation. No fundamental differences were noted in these species with respect to the histological appearance of, or the relation between, the growing bronchi and the primitive mesenchyme in which the organoid development takes place. The author demonstrates that the pulmonary mesenchyme differentiates not only into alveoli but also into the epithelium lining the bronchi. He also shows that the appearance and disappearance of intracellular glycogen distinguishes those cells involved in the differentiation process. He describes formation of alveolar walls, which are first marked by the appearance of a lining of cuboidal cells. These cells later disintegrate in situ, desquamate to leave bare capillary loops, or shrink and regress to form inconspicuous cells, referred to sometimes as "septal cells." In anterior chamber transplants, the transplants varied in their viability and ability to grow and differentiate. Those growths with good vascularization were able to duplicate the normal processes. Those with less adequate blood supply, and hence poorer nutrition, produced bizarre changes in structure of adult lung forms or resulted in overgrowth of only one of the various elements of the fetal lung tissue. The degree of differentiation varied considerably. Thus were found large amounts of cartilage, fibrous tissue, or growths of primitive mesoderm remarkably similar to a rapidly growing spindle cell tumor. The author points out the similarity of these findings to pathological conditions which are thought to arise in the adult human lung, such as bronchiectasis and congenital cysts of the lung.

HAW CHAN, San Francisco.

UNUSUAL HAMARTOMA OF THE LUNG IN A NEWBORN INFANT. CYRIL J. JONES, Arch. Path. **48**:150 (Aug.) 1949.

Hamartoma, a term coined by Albrecht in 1904, may be defined as benign "tumor-like malformations in which occur only an abnormal mixing of the normal components of the organ. The abnormality may take the form of a change in quantity, arrangement or degree of dif-

ferentiation, or may comprise all three." Hamartoma of the lungs is uncommon. The youngest age at which it has been found to occur, as reported in the literature, is 21 years. Hence, the case in a premature newborn white infant who lived one hour after birth is of interest. In this case the hamartoma occupied the entire right upper lobe of the lung, compressing the middle and lower lobes. Microscopically the tumor was composed mostly of fibrous tissue and some cartilage, fetal fat, and normally developed lung tissue. All these tissues were benign in appearance. The author feels that hamartoma of the lungs should be discoverable any time after birth because of its nature of a developmental malformation. That cases have not been reported appears to him extraordinary. If recognized as the cause of serious clinical malformations, it should be entirely amenable to surgical removal.

HAW CHAN, San Francisco.

ASTHMA IN CHILDREN: SALIENT DIAGNOSTIC PROBLEMS. BRET RATNER, J. A. M. A. **142**:538 (Feb. 25) 1950.

The broad aspects of management are discussed, with emphasis on a careful history, especially as to time of day of attacks and food diary. Examination should include roentgenography. Early skin testing is usually futile or misleading. Symptoms should be present for about a year before the skin becomes sensitized. Small doses of epinephrine, 3 to 4 minums (0.18 to 0.25 ml.), should be used. Frequently bronchoscopic aspiration is absolutely necessary for diagnosis and treatment.

KIMBALL, Evanston, Ill.

PULMONARY HAEMOSIDEROSIS. MARY WILMERS, Proc. Roy. Soc. Med. **42**:87 (Feb.) 1949.

Pulmonary hemosiderosis is reported in a girl of 2½ years.

WILLIAMSON, New Orleans.

DISCUSSION ON NON-TUBERCULOUS CONDITIONS REVEALED BY MASS RADIOGRAPHY. JAMES MAXWELL; PETER KERLEY, and THOMAS PAXTON, Proc. Roy. Soc. Med. **42**:1039 (Dec.) 1949.

The Ministry of Health Mass Radiography Unit examined 3,000,000 persons in a three-year period, 1946 through 1948. A total of 3,423 conditions requiring clinical investigations were revealed, 35% of which were nontuberculous. The latter group comprised pneumonitis, collapse of lung, sarcoidosis, and pathological conditions of the diaphragm. Cardiovascular abnormalities, including rheumatic hearts and congenital malformations, were detected, and a few cases of intrathoracic neoplasms were found. Ninety-five per cent of all roentgenograms were found to be normal.

HEARD, Monterey, Calif.

CHYLOUS PLEURISY. M. LAMY, M. L. JAMMET, M. AUSSANNAIRE, and L. CHADOUTAUD, Pédiatrie **37**:415 (July-Aug.) 1948.

A 4-month-old infant was admitted to the hospital because of coughing and vomiting for three weeks. There was a slight dulness over the right lung base. A skin test for tuberculosis showed a positive reaction. Paracentesis of the pleural space yielded a chyle-like fluid (white, milky, protein 6%, lipids 44%). Roentgenography of the chest showed right pleural effusion and a mediastinal tumor. The chylothorax disappeared in the course of a month following four pleural punctures. The mediastinal mass remained of the same size and did not respond to roentgen therapy. Gastric washings remained negative for the bacilli. There was a persistent temperature elevation. Streptomycin therapy was started, but the child died of tuberculous meningitis. Postmortem examination proved the mediastinal mass to be tuberculous lymph nodes, with caseous degeneration and compression of the thoracic duct by one of the nodes with tuberculous destruction. The esophagus was involved by the tuberculous process.

Chylothorax is a rare condition with only few cases reported in the literature. Dyspnea and cyanosis are common; the vomiting and coughing spells which occurred in this case were probably not due to the chylothorax. Dulness over the right lung base is characteristic. Trauma and congenital malformations are considered the most frequent causes of chylothorax in children, although in the case presented the cause was the compression by tuberculous lymph nodes.

GLASER, Chicago.

CIRCULATING PLASMA IN INFANTILE PNEUMONIA. V. GOTTHEINER and P. ROBINSON, Ann. pædiat. **176**:1 (Jan.) 1951.

It is questionable whether in the present state of our knowledge, we can speak of "normal values" of circulating plasma in babies. Even less can we speak of normal values for whole blood. The wide range, as found by the present writers, may be used as a basis for research, but hardly for practical ends. In none of the investigated cases of infantile pneumonia was a decrease revealed in circulating plasma.

The present writers feel that the generally accepted opinion, that certain clinical symptoms are taken to indicate a decrease in circulating plasma, is erroneous. Such a decrease is not found always in "peripheral circulatory failure" in infantile pneumonia.

The treatment by analeptic drugs in cases of pneumonia with "peripheral circulatory failure" seems to lack physiological foundation. Even the actual pharmacological effect of strychnine is missing when nontoxic doses are given. It has yet to be proved that such a pharmacological effect is of any clinical value.

FROM THE AUTHORS' SUMMARY.

A RARE CASE OF PNEUMOCHYLOTHORAX IN AN INFANT. G. B. MATTEUCCI, Arch. ital. pediat. e puericol. **14**:205, 1951.

Description is given of a case of left-sided pneumochylothorax in a 4-month-old baby with an infiltrative tuberculous lesion of the lung. The outcome was recovery. The study of the clinical course and the chemical study of specimens of fluid, obtained by many thoracocenteses, together with the alimentary lipemic curve, show definitely the chylous nature of the exudate.

FROM THE AUTHOR'S SUMMARY.

OBSERVATIONS ON RESPIRATORY FUNCTIONS WHEN THERE WAS AN ABNORMAL COMMUNICATION OF A BRONCHUS TO THE OUTSIDE. G. S. MARCHESE, Minerva pediat. **2**:162 (April) 1950.

A boy of 8 years appeared to breathe through a thoracic fistula only when there was resistance to normal expiration.

HIGGINS, Boston.

STATISTICAL STUDY ON BILATERAL PNEUMOTHORAX IN CHILDREN 5 TO 15 YEARS OF AGE. E. RUCCI, Minerva pediat. **2**:165 (April) 1950.

At a tuberculosis sanatorium in Milan 24 children were treated by artificial pneumothorax; 11 showed clinical improvement or cure, while 13 became sicker or died. The percentage of improvement was greater in children 11 to 15 years of age than in the children 5 to 10 years old.

HIGGINS, Boston.

INCIDENCE OF PRIMARY ATYPICAL PNEUMONIA. Z. HLOUŠKOVÁ and J. HOUŠTĚK, Pediat. listy **5**:20, 1950.

On the basis of 94 observations in children from 1 to 14 years, part of them admitted with the diagnosis of tuberculous lung lesions, the clinical picture and roentgenographic changes are described.

FROM THE AUTHORS' SUMMARY.

PLASMOCELLULAR PNEUMONIA. FOLKE WINELL, Nord. med. **41**:760 (April 29) 1949.

Winell reports a fatal case of plasmocellular pneumonia in a 3-month-old boy. He was admitted to the pediatric clinic of the University of Lund at 2 months of age for an obscure skin disease. During the last few days of life he suffered from respiratory distress and fever. Autopsy revealed diffusely consolidated lungs. The histologic picture was typical, with abundant interstitial cellular infiltration of plasma cells and lymphocytes. The alveolar epithelium was hypertrophic. The red pulp of the spleen was rich in plasma cells. There were scattered inflammatory infiltrates with plasma cells in the cortex of the kidneys; similar changes were found in the liver.

WALLGREN, Stockholm, Sweden.

MORTALITY OF PNEUMONIA IN CHILDREN TREATED WITH SULFONAMIDE OR PENICILLIN. GUNNAR HÖVDING, Nord. med. **42**:1397 (Aug. 26) 1949.

Of 198 children with pneumonia treated at the Aker Municipal Hospital, Oslo, 18 died (mortality rate 9.4%). Of the patients, 44 were below one year of age, and of these, 15 died (mortality rate 34.1%). If the deaths during the first 24 hours are excluded, the mortality rate was 9.4%. There was no difference between the mortality rate for patients treated with sulfonamides and the mortality rate for patients treated with penicillin.

WALLGREN, Stockholm, Sweden.

## Diseases of Gastrointestinal Tract, Liver, and Peritoneum

A STUDY OF THREE HUNDRED CASES OF DIARRHEA IN INFANTS AND CHILDREN DURING THE SUMMER AND FALL OF 1948. JULIAN D. LEVINSON and WILLIAM B. RAYCRAFT, J. Pediat. **36**:316 (March) 1950.

In 300 Chicago infants and children with diarrhea, Shigella was recovered in 28%, Salmonella in 5%, and Proteus-paracolon-Pseudomonas organisms in 46%. Shigella was found mostly in children over one year of age and Proteus-paracolon-Pseudomonas organisms mostly in children under one year. Sulfadiazine plus streptomycin given orally were most effective in specific therapy.

MACDONALD, Pittsburgh.

PNEUMOPERITONEUM IN THE DIFFERENTIAL DIAGNOSIS OF DIAPHRAGMATIC HERNIA. RICHARD C. CLAY and C. ROLLINS HANLON, J. Thoracic Surg. **21**:57 (Jan.) 1951.

The authors report the diagnostic use of pneumoperitoneum in four cases of diaphragmatic hernia. The procedure is especially useful in the differentiation of diaphragmatic hernia and intrathoracic tumors. It has also proved helpful in the diagnosis of diaphragmatic hernia when a solid organ, such as the liver, occupies the space within the hernial sac. A technique of administration of pneumoperitoneum is described.

MEYER, Chicago.

PRACTICAL TREATMENT OF THE DIARRHEAS OF EARLY LIFE. E. A. SOCOLA, New Orleans M. & S. J. **103**:266 (Dec.) 1950.

The author outlines a routine for treatment of acute gastroenteritis in infants. Fluids can be given orally, a modified Ringer's solution containing a small amount of potassium chloride being used. The author feels that the use of potassium is of paramount importance. Transitional foods and formulas to be used after the acute stage are mentioned.

MCGUIGAN, Evanston, Ill.

CONGENITAL ANOMALIES OF ESOPHAGUS. WILLIAM E. LADD, Pediatrics **6**:9 (July) 1950.

Congenital esophageal atresia, esophageal stricture, esophageal duplications, tracheoesophageal fistula, and their variations are considered in this paper. The improvement which has taken place in the last 10 years in the treatment of surviving patients with esophageal atresia is mentioned. The methods used to effect this improvement are discussed, and suggestions are made for the improvement of children's surgery in general.

The purpose of the paper has not been to present a complete treatise on congenital anomalies of the esophagus, and many details are intentionally omitted. The author's endeavor has been to use this article as a vehicle for suggestions of some of the difficulties encountered in children's surgery, and of some of the methods used to overcome them, as well as to urge the American Academy of Pediatrics to help raise the standard of children's surgery. It is Ladd's conviction that the Academy can do much to accomplish this if it wishes. It is his hope that the Academy will feel that the surgical problems of early life are related to the general welfare of children, and as such are of moment to it. He believes that the time is now ripe to recognize this.

Men who are devoting their full time to the advancement of child surgery can be found in a few medical schools in the East, Midwest and Far West. The Academy could do much in advocating that full-time research become a more widespread policy. The establishment of departments of child surgery in the medical schools of the country seems the next logical step for raising the standards of child surgery.

FROM THE AUTHOR'S SUMMARY.

OESOPHAGEAL FOREIGN BODIES. GLADYS BOYD, Canad. M. A. J. **64**:102 (Feb.) 1951.

Conclusions resulting from a study of 400 cases of esophageal foreign body are presented. Symptomatology and diagnostic procedures are outlined. Three cases of long duration, one of six years, are presented.

McGUIGAN, Evanston, Ill.

OESOPHAGO-DERMATO-OESOPHAGOPLASTY FOR CONGENITAL OESOPHAGEAL ATRESIA. DUDLEY ROSS, HAMILTON BAXTER, and HOLLIE McHUGH, Canad. M. A. J. **64**:128 (Feb.) 1951.

Diagnostic and symptomatic findings in congenital esophageal atresia are briefly outlined. A case is presented in which an extra thoracic esophagus was created by tube grafting.

McGUIGAN, Evanston, Ill.

A REVIEW OF FIFTY CASES OF INTUSSUSCEPTION. W. W. JOLLY, Clinical Rep. Adelaide Child. Hosp. **1**:218 (May) 1949.

Fifty successive cases of intussusception are discussed, with attention to etiology and clinical features. Ten patients died, and their cases are reviewed with attention to the cause of death. Measures to reduce the 20% mortality rate are discussed.

McGUIGAN, Evanston, Ill.

ULCERATIVE COLITIS IN CHILDREN. J. COVERNTON, Clin. Rep. Adelaide Child. Hosp. **1**:230 (May) 1949.

Seven cases of ulcerative colitis are reviewed. Surgical treatment is not advocated. General medical management is advised, no specific measures being available.

McGUIGAN, Evanston, Ill.

THE TREATMENT OF LARGE OMPHALOCELES. L. MACE DAVID, South African M. J. **23**:755 (Sept. 10) 1949.

A case is presented, and the operative technic of Gross is described.

McGUIGAN, Evanston, Ill.

LIVER DAMAGE IN GASTRO-ENTERITIS. BERNARD SCHLESINGER, W. W. PAYNE, and E. D. BURNARD, Arch. Dis. Childhood **24**:15 (March) 1949.

Jaundice is an uncommon but well-recognized complication of gastroenteritis and a very serious condition. Evidence has been produced that liver damage may arise from severe metabolic disturbances which follow acute states of nutritional failure. Extreme examples of the condition are recognized by jaundice, enlargement of the liver, and hemophilia (hemorrhagic diathesis). Edema is often present. Variations have been observed in the clinical picture, and milder forms are mentioned. Postmortem investigations so far undertaken reveal two main pathological features: cell damage and necrosis or fatty infiltration; but further studies are needed to elucidate the exact nature and order of events in the liver.

It is suggested that protein deprivation is chiefly responsible for the pathological changes in the liver, and the excellent clinical response obtained when it is supplied in an assimilable form is in favor of this theory. Dehydration and loss of potassium are also thought to play their part in the pathogenesis, and restoration of fluid, electrolytes, and this salt in particular is an essential part of the treatment. Administration of casein hydrolysate by mouth has proved an efficient method of providing the necessary protein when other forms requiring digestion were not tolerated. On occasion recourse had to be had to the intravenous route. This involves the serious danger of infection, and a method has been described to prevent such an occurrence.

KELLY, Milwaukee.

AROBON IN THE TREATMENT OF INFANTILE GASTRO-ENTERITIS: A CLINICAL TRIAL. DAVID BEYNON, Arch. Dis. Childhood **24**:41 (March) 1949.

A new therapeutic agent, prepared from the carob bean is described. A short history of its discovery and of previous reports of its use are given, followed by a description

of its trial on patients admitted to a gastroenteritis unit over a period of six months. The conclusions drawn do not confirm previous reported results, but it is considered that further trials are indicated in primary gastroenteritis, as it might well prove useful in early cases of this type.

KELLY, Milwaukee.

EPIDEMIC GASTRO-ENTERITIS OF INFANTS IN ABERDEEN DURING 1947. C. GILES, G. SANGSTER, and J. SMITH, Arch. Dis. Childhood **24**:45 (March) 1949.

An outbreak of gastroenteritis lasting for the greater part of the year 1947 is described. Of a total of 415 infants who came under observation, for 207 the diagnosis was infective gastroenteritis; and of these, 105, or 50.6%, died. The children most affected were bottle-fed babies under 7 months, and the peaks of the epidemic occurred in April and July.

Institutional outbreaks were a marked feature of the epidemic, and the occurrence of six definite ward outbreaks is recorded. The incidence of these nosocomial cases emphasizes the infective nature of the disease.

Postmortem examination in 55 fatal cases showed once again the indefinite pathologic change associated with this disease. The changes that occurred in the intestines were often minimal, but more frequently the liver was affected to a greater or less extent, and the damage varied from slight fatty degeneration to generalized fatty changes and necrosis with little healthy liver parenchyma remaining. There were manifestations of toxic action on the kidneys but no evidence of a virus infection in the central nervous system.

KELLY, Milwaukee.

COELIAC DISEASE: A RELATION BETWEEN DIETARY STARCH AND FAT ABSORPTION. WILFRID SHELDON, Arch. Dis. Childhood **24**:81 (June) 1949.

In a group of 15 children with celiac disease the withdrawal of starch from the diet was accompanied with a rise in fat absorption that averaged 15%. The figure of 15% in this investigation is of high statistical significance. The starch-free diet enabled the children to tolerate virtually a normal fat intake and led to improvement in weight, character of the stools, and temperament.

A four-day period for a fat balance is too short when fat absorption is defective. Although a 12-day period was employed in this investigation, an eight-day period would have been sufficient. Estimations of fecal fat alone do not provide a reliable index of the fat absorption.

KELLY, Milwaukee.

SOME ETIOLOGICAL FACTORS IN THE COELIAC SYNDROME. ALAN BROWN, Arch. Dis. Childhood **24**:99 (June) 1949.

The author states that it must be apparent from the studies made that very little has actually been added to our knowledge of this disease. However, they have served to reemphasize the fact that much of the knowledge of this disease as recorded by the earliest writers on the subject is being proved again. Particularly one is impressed by the presence of infection at the onset of this disease and by improper feeding during infancy and childhood.

The preliminary results of the dental survey indicate that the well-known clinical observation —that children who have suffered from celiac disease and have had proper dietary control are blessed with better than average teeth—is probably true. The genetic investigation has thrown some light on the probable relation of celiac disease to diabetes and a possible pancreatic dysfunction of some type. In experimental studies with animals the factor of infection has been emphasized and would appear to be a very important one. The relation of vitamin B complex to the prevention and relief of the celiac syndrome deserves further investigation. The cause of this condition can apparently be solved only by continued, cooperative effort in numerous branches of medical science.

KELLY, Milwaukee.

SARCOIDOSIS. URSULA JAMES, Proc. Roy. Soc. Med. **42**:85 (Feb.) 1949.

The patient, aged 9 years, had been repeatedly absent from school for four months because of mumps. On examination bilateral, symmetrical, nontender enlargement of the parotids and

general enlargement of lymph nodes (neck, axillas, groins, epitrochlears) were found. There was also moderate enlargement of liver and spleen. Lymph node biopsy gave a histological picture of sarcoidosis, which is very rare in childhood.

WILLIAMSON, New Orleans.

PRESENT STATE OF TREATMENT OF MALIGNANT TUMORS OF THE SMALL AND LARGE BOWELS AND THE RECTUM IN CHILDREN. M. GUILLEMINET and J. JACQUET, Pédiatrie **37**:121 (Jan.-Feb.) 1948.

One hundred eighty-three cases of malignant tumors of the intestinal tract are reviewed. The prognosis is generally bad, 21.6% of patients dying of postoperative shock, and even so surgery does not always avoid recurrences. Early diagnosis offers the best hope for the patient, but the nonspecific symptoms of abdominal pains, diarrhea, and loss of appetite usually do not lead to the thorough examination in children that we are used to performing in the adult. The diagnosis may be facilitated by the recognition of a frequent complication—ileocecal intussusception—which occurred in one-third of the patients in whom the tumor was located in the terminal ileum, cecum, or ascending colon and which should always lead to a thorough study of the patients by means of roentgenograms. Adequate care before, during, and after surgery can further reduce the high immediate postoperative mortality due to shock.

GLASER, Chicago.

ETIOLOGY OF LIVER CIRRHOSIS OF INFANTS AND CHILDREN. J. CHAPTAL and E. DE MARMIER, Pédiatrie **37**:316 (May-June) 1948.

Biopsy by needle puncture has permitted histologic study of livers before the pathologic changes have progressed to a point where recognition of the initial form of the lesion is impossible. Toxic causes of cirrhosis (alcoholism, spices) do not play an important etiological role in children. Infectious causes of a secondary nature (syphilitic, tuberculous, parasitic) are not as important as primary hepatic infections due to hepatotropic viruses. Serial studies on the early stages of the last type of cirrhosis were possible by means of puncture biopsy. Constitutional and congenital causes have been assumed to play a role because of the early occurrence of cirrhosis in certain cases in the absence of any known preceding infection. Among these factors are Rh incompatibility and biliary stenosis or atresia, and certain congenital and familial cases occur for which no explanation can be found at present.

GLASER, Chicago.

PIERRE MAURIAC SYNDROME—GLYCOGENOSIS AND HEPATOMEGALY. R. HOUET, Presse méd. **57**:159 (Feb. 19) 1949.

The author discusses this rather rare complication of inadequately treated diabetes. Since Mauriac's original description of the syndrome, 36 examples have been added to medical literature.

DAFFINEE, Melrose, Mass.

THE CHOLINERGIC MECHANISM OF INTESTINAL INTUSSUSCEPTION. H. LABORIT, Presse méd. **57**:223 (March 12) 1949.

In the course of investigation of the causes of intestinal infarcts, the author produced invagination of the intestine by the local application of acetylcholine to the intestine. Other observers have described the production of intussusception by intravenous administration of acetylcholine.

Accordingly, the author used atropine in two clinical cases of intussusception, as an adjunct to manual reduction. Immediate reaction resulted in the intestinal wall, and the normal appearance was restored. The author speculated that the mechanism involved seems to implicate some underlying factor, such as vitamin deficiency or allergy.

DAFFINEE, Melrose, Mass.

CHANGES IN THE CIRCULATION IN TOXICOSIS. CIHAD TAHSIN GÜRSON, Helvet. paediat. acta **5**:489, 1950.

A number of children suffering from toxicosis were examined routinely by roentgenography, blood pressure study, and electrocardiography. The results obtained by the present author do not fully agree with the hitherto accepted findings.

In 81.5% of all cases the blood pressure was raised, by 34.8% in 30% of the cases and by 15 to 3.30% in 46.5% of the cases. The blood pressure remained almost normal in 16% of the cases, and it had dropped by 15% in 4.7% of cases. Pathological changes were shown in 79.5% of cases in the electrocardiogram, e. g., the main finding was a negativity in the preterminal part of the T wave; there were a depression of the ST segment (51.5%) and a prolongation of the Q-T interval (60%). In some cases (12.5%) the spread of excitation was delayed, and in a few (9%) a partial block was present. As the toxic condition and blood pressure improved, all these changes in the electrocardiogram disappeared completely.

On x-ray examination one observes a heart of diminished size, the latter being a well-known phenomenon. The investigation tends to show that toxicosis is a disease which is accompanied with a considerable increase in blood pressure, which imposes great strain on the circulatory system.

FROM THE AUTHOR'S SUMMARY.

UNILATERAL PAROTITIS IN A NEWBORN FULL-TERM BABY. G. BALLARÉ, Lattante **21**:240 (April) 1950.

An infant was born with a nonsuppurative unilateral parotitis; the puerperium and parturition had been normal, and lactation developed normally. Treatment was by penicillin; recovery was uneventful. The cause was unestablished.

HIGGINS, Boston.

ADRENAL CORTEX DEFICIENCY IN CELIAC DISEASE. E. SCHWARZ-THIENE, Minerva pediat. **2**:149 (April) 1950.

Two cases of infantilism in celiac disease were studied. The behavior of blood sugar curves and of the electrolytes in the plasma suggest strongly a deficiency of the adrenal cortex in these cases.

HIGGINS, Boston.

SPECIFIC ACUTE PERITONITIS IN INFANCY. L. GUBERN SALISACKS, Acta pediat. españ. **97**:27 (Jan.) 1951.

Salisacks presents 12 cases of specific peritonitis due to tuberculosis and streptococcic, gonococcic, and pneumonic infections and mentions the difficulties they present in the differential diagnosis. All these conditions frequently may be confused with acute appendicitis in the infant and young child.

With the sulfonamides and antibiotics, the need for surgery has been greatly diminished, and if there is the least bit of uncertainty as to the diagnosis, a small right incision is made in the right iliac fossa, and bacteriological study done on the pus before more surgery is done. Drainage is done, and the antibiotic indicated for the specific organism is given. Removal of the appendix and other surgery is done if the need is found.

The author emphasizes the need for a careful history, as the antecedent illnesses are of great importance in the proper diagnosis. He feels that in very severe, often neglected cases, the mortality is much lower with this form of treatment. He includes roentgenograms showing the use of the Harris sound in cases with suspected obstruction.

ALLEN, Santa Fe, N. M.

POSTOPERATIVE LIVER ABSCESS. ALEJANDRO AGUIRRE, FRANCISCO BELTRAN, and RUBEN LAVALLE, Bol. med. Hosp. inf., México **7**:894 (Dec.) 1950.

The outstanding facts of the case under discussion were (1) the roentgenographic finding, without clinical data, of a hepatic abscess in full formation; (2) the rareness of hepatic abscesses as postoperative complication, even in massive peritoneal processes; (3) the formation of the abscess during prolonged administration of antibiotics and sulfadiazine in sufficient doses, and (4) the favorable resolution, with disappearance of the fever in 24 hours and the roentgenographic image in 20 days, when emetine and chloroquine were substituted for the previous therapeutics. The evolution very strongly suggests amebic etiology even in the absence of colic.

FROM THE AUTHORS' SUMMARY.

PHARMACODYNAMIC EFFECT OF STREPTOMYCIN ON INTESTINAL TRACT (CONTRIBUTION TO THE THEORY OF TREATING NUTRITIONAL DISORDERS OF INFANTS WITH STREPTOMYCIN). J. STROEDER and K. SIMON, Arch. Kinderh. **137**:236 (Nov.) 1949.

Loops of the intestines of mice, rats, and guinea pigs in vivo and in surviving preparations were perfused with solutions of penicillin and of streptomycin. The influence of each antibiotic on the intestines was studied after application of acetylcholine, histamine, barium chloride, and the toxin on Bacterium coli. The records revealed no influence of penicillin on movements of the intestines, but after perfusion with streptomycin a definite antitoxic action against the toxic action of acetylcholine, histamine, and the toxin of B. coli was evident.

ARON, Chicago.

PROBLEM OF GENESIS OF MECONIUM ILEUS. W. ZIESCHKA, Arch. Kinderh. **138**:1 (Dec.) 1949.

The autopsy findings in a third case of meconium ileus confirmed the observation that, as in the first two cases examined, the small and the large intestines were much shorter than those in normal infants (139 and 33 cm. respectively, as compared to 277 and 42 cm. respectively in the norm). The mesenteric plexus in all three cases showed histological changes similar to those found in spastic ileus of the adult.

In the third infant, who died at the age of 8 days, the author was able to demonstrate histologically severe degenerative changes in the region of the dorsal nucleus of the vagus nerve, in the substantia reticularis, and in the nucleus ambiguus. The ganglion cells of the other nuclei of the pons and of the olives in the medulla oblongata were found to be normal. The nuclei in the medulla oblongata which revealed the degenerative changes are just those which, by way of the vegetative nervous system, regulate the innervation of the intestines.

The author concludes that the degenerative changes of the ganglion cells, superimposed on the processes in the intestinal tract, are the primary cause of the disease. The diseased ganglion cells provoke a continual spasm in the region of the large intestines which are innervated by the vagal nerve. This continual spasm causes stagnation of the meconium, formation of a meconium plug, and eventually ileus.

ARON, Chicago.

LATER EXAMINATIONS AFTER OPERATION IN CASES OF MEGACOLON. W. TONNIE and A. HERINK, Deutsche med. Wchnschr. **9**:265 (March 2) 1951.

The operation consisted in resection of the presacral nerve and denervation of the inferior mesenteric artery. This operation was done in eight boys aged 4 to 12 years and three adults. The children were seen again after a lapse of a few months to about three and one-half years. In some cases the ureters were also somewhat dilated. For some patients the result was very good; others needed some laxative.

AMBERG, Rochester, Minn.

AN EPIDEMIC OF INFANTILE DYSPEPSIA IN 1948. A. MORES, M. JADRNÍČEK, and R. ČOUDKOVÁ, Pediat. listy **5**:14, 1950.

A survey of the death rate of infants treated at the children's clinic in Olomouc during the last five years is given, and the percentage of those deaths caused by diarrhea is stated. The falling tendency of the mortality was suddenly interrupted by a sharp rise in 1948. It rose to 50% of all children treated for diarrhea during the spring months. It was a regional epidemic, and it is feared that 31 of the children who died might have been infected at the hospital, where they had originally been admitted for some other disease; most of them were fully or partly breast-fed. The clinical picture, the bacteriologic examination of the stools, and the necropsy are fully described.

FROM THE AUTHORS' SUMMARY.

DIARRHEA IN INFANTS. F. VANIČEK, A. VLČEK and J. DANIEL, Pediat. listy **5**:71 (No. 2) 1950.

The bacteriological analyses of about 2,000 samples of stools of infants, both healthy and sick, show that infantile diarrhea most frequently occurs when the coli strains present in the intestine have a weak antagonistic power against other bacteria of normal intestinal flora, particularly

against Proteus vulgaris, which is almost always present in the intestinal tract. If the coli strain is powerfully antagonistic, P. vulgaris is kept under control and is latent. If the coli strain is weak, P. vulgaris or other intestinal bacteria increase and cause trouble.

The methods to measure the antagonistic power of coli strains against other intestinal bacteria, especially what the authors call the "barrier test" of its antagonistic power against P. vulgaris, are elaborated on. Extraordinarily powerful coli strains were found which did not allow P. vulgaris to pass the first or second barriers.

Extraordinarily powerful coli strains were used for the treatment of infantile diarrhea with the intention of reestablishing the coli rule in the intestine. Living, antagonistically powerful coli strains reached the intestine easily, and most permanently, and quickly overruled the intestinal flora; the clinical signs of infantile diarrhea retreated quickly. Detailed results are reported in the second part of this paper.

The question of the pathogenicity of the coli bacteria will be treated in the following publication.

FROM THE AUTHORS' SUMMARY.

## Nervous Diseases

MEDICAL TREATMENT OF EPILEPSY TODAY. JOHN S. GARVIN, Illinois M. J. **98**:344 (Dec.) 1950.

Five hundred cases of epilepsy have been reviewed with respect to type of clinical seizure, electroencephalographic findings, and response to anticonvulsant medication.

Grand mal attacks were found in 33.8%, psychomotor attacks in 11.4%, Jacksonian seizures in 7.8%, and petit mal attacks in 2.4%. In 42.6% of the series there was more than one type of seizure (grand mal and psychomotor seizures were commonest). Two per cent were atypical.

Almost 20% of patients with only grand mal seizures had normal electroencephalograms, while none of those with both grand mal and petit mal attacks had normal brain wave patterns.

Forty-seven per cent of patients with grand mal seizures were free of attacks with suitable medication, while only 10% of those with psychomotor seizures could be completely freed of attacks.

The prognosis as to control of seizures depends on the type and frequency of clinical attacks and the electroencephalographic findings.

Combinations of anticonvulsant medications appear to be more effective than any single drug.

The various types of anticonvulsant drugs and combinations of drugs are discussed, and their toxic effects are noted.

A higher percentage of improvement in the control of epileptic seizures may be obtained with individualized dosage and appropriate combinations of anticonvulsant drugs.

BARBOUR, Peoria, Ill.

AUREOMYCIN IN THE TREATMENT OF INFLUENZAL MENINGITIS. MILES E. DRAKE, J. EDMUND BRADLEY, JEROME IMBURG, FRED R. MCCRUMB JR., and THEODORE E. WOODWARD, J. A. M. A. **142**:463 (Feb. 18) 1950.

Seven patients with influenzal meningitis were treated with aureomycin alone. All recovered. Ages ranged from 5 months to 3½ years. If the patient was unconscious, the intravenous route was used, 100 mg. initially and 50 mg. every four to six hours; otherwise, the dose was given orally, usually 750 mg. initially and 250 mg. every four hours.

KIMBALL, Evanston, Ill.

THE CLINICAL SIGNIFICANCE OF THE STRETCH REFLEX IN SPEECH REEDUCATION FOR THE SPASTIC. PATTI FOTHERGILL and ROBERT HARRINGTON, J. Speech & Hearing Disorders **14**:353 (Dec.) 1949.

The authors suggest that the goal in spastic paralysis should be reduction of time of movement beyond the threshold of the elicitation of the stretch reflex. Teaching voluntary control is a misconcept which should be corrected on the basis of the actual facts.

PALMER, Wichita, Kan.

LETTER TO THE PARENTS OF THE CEREBRAL PALSIED CHILD. MARY HUBER, J. Speech & Hearing Disorders **15**:154 (June) 1950.

In the form of a letter to the parents the author covers items of explanation relative to speech for parents of cerebral palsied children.

PALMER, Wichita, Kan.

POSTINFANTILE CORTICAL HYPEROSTOSIS WITH SUBDURAL HEMATOMA; REPORT OF CASE AND REVIEW OF LITERATURE. BEDFORD H. BERREY, Pediatrics **6**:78 (July) 1950.

The coexistence of postinfantile hyperostosis and subdural hematoma, an association hitherto unreported, is described in a child 29 months old, and a brief review of the 32 previously reported cases of infantile and postinfantile cortical hyperostosis is presented.

The cause of the syndrome is not known, but hereditary, infectious, traumatic, allergic, and hematologic factors have been considered. Hypervitaminosis A appears to be a definite etiologic possibility in the postinfantile form.

Hyperirritability, fever, and anemia with leucocytosis are the outstanding clinical manifestations; characteristic shadows of external thickenings of the cortex of the bones are pathognomonic.

Since the course of the disease is self-limited, treatment is directed toward symptomatic relief and reduction of intake of vitamin A when it has been excessive.

FROM THE AUTHOR'S SUMMARY.

DIASTEMATOMYELIA (CONGENITAL CLEFTS OF SPINAL CORD): DIAGNOSIS AND SURGICAL TREATMENT. DONALD D. MATSON, ROBERT P. WOODS, JAMES B. CAMPBELL, and FRANC D. INGRAHAM, Pediatrics **6**:98 (July) 1950.

Diastematomyelia associated with the presence of a bony spicule arising from the posterior aspect of a vertebral body and transfixing the spinal cord or cauda equina has been encountered in 11 operative cases. In the last nine of these the diagnosis was made previous to operation.

It seems apparent that progressive neurologic impairment of the lower extremities and of the rectal and vesical sphincters may result from increasing distortion of the neural axis as a result of fixation produced by these bony spicules during the growth period.

The diagnosis is suspected in the presence of cutaneous midline defects, muscular imbalance in the lower extremities, gait disturbances, deformities of the feet, urinary or fecal incontinence, or increasing enuresis. The diagnosis is confirmed on roentgenologic examination by the presence of a midline opacity usually in the region of a spina bifida or other vertebral anomaly or by visualization of two separate subarachnoid channels on myelography.

Operative treatment consists in laminectomy with extradural removal of the bony spicule so far as possible, followed by opening the dura with excision of its reflections adjacent to the spicule, excision of the remaining bony prominence down to the anterior dura, and division of all adhesions to the bifid cord or cauda equina until the latter is freely movable within a single dural canal.

In all these cases there appeared to be complete division of the cord or cauda equina into separate parts rather than reduplication of the cord. Each half of the neural axis was invested with its own meninges.

The operative findings in the 11 cases reported here, together with the brief follow-up observations noted to date, have convinced the authors that it constitutes good preventive medicine to carry out surgical treatment of diastematomyelia associated with spina bifida occulta at any time the diagnosis is made during infancy and childhood.

FROM THE AUTHORS' SUMMARY.

THE CHANGING INCIDENCE OF CONVULSIONS IN CHILDHOOD. ROBERT A. SHANKS, Arch. Dis. Childhood **24**:212 (Sept.) 1949.

The seasonal and age incidences of convulsions in children under 3 years of age have been investigated for three five-year periods, 1922 to 1926, 1932 to 1936, and 1942 to 1946. The results demonstrate the characteristic curves of tetany in the first two periods with their virtual disappearance in the last. From this it is concluded that in Glasgow hypocalcemia was the

predominant etiological factor in convulsions in the earlier periods under investigation, but is so no longer. The total and relative incidence of convulsions in infancy and childhood has not been reduced by this fall in the incidence of hypocalcemia.

KELLY, Milwaukee.

THE STURGE-WEBER SYNDROME. CHRISTOPHER STRANG, Edinburgh M. J. **56**:409 (Sept.) 1949.

Strang reports a case of the Sturge-Weber syndrome in a 15-year-old girl. Anticonvulsant therapy (phenobarbital) resulted in mild clinical improvement. Roentgen therapy resulted in dramatic improvement.

MACDONALD, Pittsburgh.

ENCEPHALOMENINGOCELE TREATED SUCCESSFULLY BY PLASTIC SURGERY. G. LAZORTHES, F. DEODATI and P. PAGE, Presse méd. **57**:3 (Jan.) 1949.

Encephalomeningoceles may be classified according to their location: occipital, sincipital, or anterior. The anterior group is divided into three types: frontonasal, nasopharyngeal, and spheno-orbital. The procedure for correction of the frontonasal type is described and is illustrated by a case report.

DAFFINEE, Melrose, Mass.

TREATMENT OF SPINA BIFIDA WITH ULCERATION. G. BIANCHI, Lattante **20**:431 (July) 1949.

A newborn baby with spina bifida and meningocele with ulceration was operated upon and the sac removed and the wound closed. Three weeks later it was observed that the head was enlarging in size. X-ray therapy directed at the choroid plexuses was given. When the child was seen at the age of 6 months, the hydrocephalus had been checked.

HIGGINS, Boston.

TREATMENT IN A CASE OF PNEUMOCOCCIC MENINGITIS IN AN INFANT. F. COPELLO, Lattante **21**:232 (April) 1950.

An infant of 5 months with pneumococcic (type I) meningitis failed to respond favorably to penicillin-sulfathiazole or streptomycin therapy. After spinal drainage, intrathecal administration of 1 gm. of a tetrasulfonamide preparation (sulfanilamide 0.2 gm., sulfathiazole 0.2 gm., sulfadiazine 0.3 gm., sodium sulfamethazine 0.3 gm.) in 20 cc. was begun. One and one-half hours later, the child had convulsions; after coming out of the convulsive state, recovery was rapid, no other antibiotic being given except penicillin intramuscularly.

HIGGINS, Boston.

PNEUMOCOCCIC MENINGITIS IN CHILDREN. L. CARTAGENOVA, A. GHIO, and F. COPELLO, Lattante **21**:705 (Nov.) 1950.

Of 271 patients with meningitis treated at the children's medical clinic in Genoa, in 42, or 15%, the disease was found to be due to Pneumococcus. Twenty-three cases (18 deaths) were due to type I and 16 cases to type III. Twenty-eight were secondary to infections of the nasopharynx or respiratory tract (16 deaths), and 14 were seemingly primary in the meninges (11 deaths). Twenty-nine cases were acute, nine subacute, and four chronic. Of the 25 infants with open fontanels, 19 died, and only 8 of the 15 infants and children with closed fontanels died. The best results were obtained by combining sulfonamide and penicillin medication.

HIGGINS, Boston.

ACUTE CEREBELLAR ATAXIA. A. M. CAVALLOTTI, Minerva pediat. **2**:510 (Oct.) 1950.

Encephalitis developed in a girl of 8 years 10 days after an attack of rubella. The onset was acute with temporary blindness, severe headaches, dysarthria, opisthotonus, and general weakness. The spinal fluid showed 148 cells, mostly lymphocytes, and a positive Pandy reaction. Later anisocoria, nystagmus, and the typical findings of cerebellar ataxia appeared. Recovery was slow, but was apparently complete at the end of six months.

HIGGINS, Boston.

TIC NEUROSIS IN CHILDHOOD. B. LORAND, Paediat. danub. **6**:203 (Oct.-Dec.) 1949.

In the introduction Lorand discusses a more recent view of the origin of child neuroses, which is based upon the following factors: (1) greater vulnerability of the nervous system and difficul-

ties of adaptation owing to a dysharmonic course of development; (2) the fixation of inadequate mechanisms of conditioned reflexes. Formerly, hereditary factors and early trauma were usually considered to be responsible.

After surveying the literature of tic neurosis with special regard to its pathogenesis and therapy, the author reports on her own investigations and results. She observed and treated 108 patients, and fully examined 42, and her findings are as follows:

In the majority of less serious cases infantile and narcissistic traits are apparent and in such cases the tic generally arises by way of conditioned reflex mechanisms. In graver cases of tic neurosis, however, some characteristic traits of obsessional neurosis, for example, a trend to be overprecise, and a heightened feeling of responsibility, are present to an unusually high degree. The debility of the motor system (the Oseretzky motor test was applied in all cases) could not be ascertained, and consequently, the assumption of organ inferiority must be ruled out.

In treatment, rhythmical and inhibitional gymnastic exercise, electrotherapy, and psychotherapy were varied and combined according to individual needs, with such good results that the pessimistic view of some of the earlier workers cannot continue to be upheld.

Six cases which represent different pathogenetic groups are analyzed in detail.

In concluding, the author reviews some of the latest observations made in this field, and from her own experience states that grave forms of functional tic neurosis are infantile and early manifestations of later obsessional neuroses. Children afflicted with tic, therefore, need special care and guidance.

FROM THE AUTHOR'S SUMMARY.

CSF COLLOID CURVES IN PURULENT MENINGITIS TREATED WITH PENICILLIN. I. VINCE, Paediat. danub. **6**:275 (Oct.-Dec.) 1949.

The benzoic reaction in the cerebrospinal fluid of 22 children suffering from purulent meningitis was serially observed. From the study it was concluded that at the onset of the disease the colloid curves show a mirror image of a somewhat broadened normal curve. In patients responding well to treatment, a change occurs within the first few days, as if the curve revolves round its axis. In cases with slow recovery and neurological manifestations, the curves become irregular and do not regain their original shape. Although the precise mechanism of the phenomena is still unknown, the above signs still seem to have some prognostic value.

FROM THE AUTHOR'S SUMMARY.

SIGNIFICANCE OF ALBUMINO-CYTOLOGICAL DISSOCIATION. L. BARTA and F. GERLOCZY, Paediat. danub. **6**:240 (Oct.-Dec.) 1949.

Cases with albuminocytological dissociation in the cerebrospinal fluid, occurring in groups, are reported in Hungary. Most of them appeared at times when there were no cases of poliomyelitis. The clinical course was benign, with hardly any complications. There were also some cases of infantile diarrhea in which albuminocytological dissociation could be found. In the patients there were no conspicuous nervous symptoms or none at all.

It seemed from the observations that a neurotropic virus other than that of poliomyelitis was responsible for the disease. In most cases there were few symptoms, but the cerebrospinal fluid yielded the characteristic albuminocytologic dissociation from the onset. It seemed that the Guillain-Barré forms of polyradiculitis might often occur without symptoms or display those of meningitis alone. In the latter cases, the dissociation could last many weeks after the patients had seemingly recovered. According to the authors' observations, viral diseases showing the syndrome of Guillain-Barré occur more frequently at periods when poliomyelitis and serous meningitis are epidemic.

FROM THE AUTHORS' SUMMARY.

NEUROLOGICAL AND REFLEXOLOGICAL EXAMINATION IN NEWBORNS AND INFANTS. JIŘÍ VÍTEK, Pediat. listy **5**:10, 1950.

The author gives a survey of the development and function of the nervous system and the methods of examination. A detailed description of reflexes at this age level and their evaluation is given.

FROM THE AUTHOR'S SUMMARY.

PSEUDOMONAS AERUGINOSA MENINGITIS IN A TWO-MONTH-OLD INFANT. A. FABER, Pediat. listy **5**:38, 1950.

Faber describes a case of Pseudomonas aeruginosa meningitis with a lethal course.

FROM THE AUTHOR'S SUMMARY.

TREATMENT OF PNEUMOCOCCAL MENINGITIS IN CHILDREN. J. HNATEK, Pediat. listy **5**:169 (No. 3) 1950.

Nine children with pneumococcal meningitis, seven of whom were admitted in a state of deep unconsciousness, were treated with penicillin intrathecally and systemically and large doses of sulfonamides. The mortality was 25%. All patients with primary meningitis recovered completely. The strikingly rapid response to penicillin intrathecally if administered during the first stage of the illness is pointed out. Attention is drawn to the frequency of a so-called second stage, a stage of abscess formation (Švejar), and to the response to penicillin thecally administered even in this second stage.

FROM THE AUTHOR'S SUMMARY.

AUREOMYCIN TREATMENT IN A NEWBORN PREMATURE INFANT WITH BACILLUS COLI MENINGITIS. G. LAURELL, J. H. MAGNUSSON, and B. WERNER, Acta pediat. **40**:174 (March) 1951.

A report is given of a case of acute meningitis caused by Escherichia coli in a newborn premature infant with scleredema. The coli strain was isolated. It proved to be very sensitive to aureomycin and was also studied from the aspect of its serological properties. The infant was treated with aureomycin, with good clinical effect.

FROM THE AUTHORS' SUMMARY.

NEUROSURGICAL ASPECTS OF ACUTE AND CHRONIC MENINGITIS. H. VERBIEST, Maandschr. Kindergeneesk. **13**:187, 1950.

The neurosurgical aspects of acute purulent meningitis and of tuberculous meningitis are discussed, with special regard to the experiences gathered in the neurosurgical department of Utrecht. Intrathecal medication implies certain dangers, while diffusion into the subarachnoidal spaces may be incomplete. Among the complications of meningitis, special attention has been paid to ependymitis and to persisting basilar meningitis. These complications do not necessarily occur simultaneously. More insight into the problems of ventriculitis is needed; this lesion is not always combined with ventricular block; in some cases, the ventricular fluid is sterile, and sometimes an absolute or relative intraventricular hypotonia is found. Rebellious traumatic meningitis as a rule is sustained by local traumatic or infectious tissue changes, or by complications as mentioned in nontraumatic meningitis.

The results of the neurosurgical treatment of postmeningitic blindness and of postmeningitic hydrocephalus have been disappointing.

In our opinion early neurosurgical treatment of tuberculous meningitis is needed until more powerful antibiotics are at our disposal.

Permanent ventricular drainage has been employed not only in cases with "acute" hydrocephalus, but in every case in which hypertensive hydrocephalus has been found. Streptomycin was applied by the intramuscular and intralumbar routes, and through intraventricular and intracisternal drains. Twenty-two patients with tuberculous meningitis have been treated by these measures; 10 patients are still alive, among which seven are surviving 9 to 15 months after the operation. Most of these patients had previously been treated unsuccessfully by intramuscular and intrathecal medication. Some contraindications to operative treatment are discussed.

FROM THE AUTHOR'S SUMMARY.

## Diseases of Genitourinary Tract

UNDESCENDED TESTES. W. H. SNYDER, JR., WILLIAM VAN VALIN, and LAWRENCE CHAFFIN, California Med. **72**:239 (April) 1950.

Orchiopexy was performed upon 152 patients. Follow-up observation was inadequate, but of known results 14% were poor.

As an increasing number of investigators have observed spontaneous descent of undescended testes, this possibility should be considered in weighing indications for operation on boys before the age of puberty. Coexisting clinically demonstrable hernia (59% in this series) is an indication for early operation. Otherwise, orchiopexy may best be delayed, perhaps until the 12th year. This was done in 25% of the patients in this series.

Three methods of operation were used, the Torek, the Cabot-Nesbit, and the Bevan. There were fewer poor results with the Torek than with the Cabot-Nesbit procedure. The greatest number of poor results were reported in cases in which the Bevan technique was used.

PRYOR, Redwood City, Calif.

ANTIHISTAMINES IN TREATMENT OF ACUTE GLOMERULONEPHRITIS. L. SALMI and D. GOTTI, Clin. pediat. **31**:643 (Dec.) 1949.

Glomerulonephritis has frequently been regarded as an allergic manifestation; therefore, it has seemed in order to try the therapeutic effect of an antihistamine drug in the treatment of 10 children with the disease. Comparing the patients treated with an antihistamine drug, autazoline (antistine®) hydrochloride with 10 control patients treated in the usual manner, the authors noted that the illness, hematuria, and albuminuria were of shorter duration in the antihistamine-treated group.

HIGGINS, Boston.

## Psychology and Psychiatry

DYSLEXIA FROM PHYSICAL VIEWPOINT. GEORGE E. PARK, Illinois M. J. **97**:30 (Jan.) 1950.

In this paper the author carries out his purpose in presenting certain broad aspects of the problem of dyslexia. He outlines the influence of some psychophysiological elements involved in reading difficulties, and discusses the predominant physical findings in 215 cases of dyslexia under treatment. The complete material is too detailed for adequate abstracting.

BARBOUR, Peoria.

DOES GLUTAMIC ACID ADMINISTRATION INFLUENCE MENTAL FUNCTION? HAROLD G. LOEB and READ D. TUDDENHAM, Pediatrics **6**:72 (July) 1950.

Thirty-three feebleminded persons, mostly adolescents and without epilepsy or other neurologic involvement, were divided into two groups well-matched as to intelligence quotient, sex, age, and type of feeblemindedness. Patients in one group received 24 gm. daily of monosodium glutamate orally for 17 weeks. Patients in the other group served as controls and received a placebo given at the same time and in like manner. Throughout the entire period of the investigation, experimental and control patients were in the same institution, on the same regimen, and received the same care and diet, which was prepared in a central kitchen.

The psychological tests administered before and after the experimental period were Stanford-Binet (Form L before and Form M after), Cornell-Coxe Performance Ability Scale, Porteus Maze, Thurstone, Thurstone Primary Mental Abilities, and Rorschach.

On the basis of detailed statistical analysis employing the method of covariance, no significant difference between control and experimental subjects could be shown, and it was therefore concluded that a beneficial effect of glutamic acid in the treatment of feeblemindedness has not been demonstrated.

FROM THE AUTHORS' SUMMARY.

## Diseases of Ductless Glands; Endocrinology

BIOCHEMICAL EFFECTS OF SEX HORMONES IN ADRENALECTOMIZED RATS. KENNETH W. BUCHWALD, LEONA HUDSON and JOSEPHINE BELLANCA, Endocrinology **47**:228 (Oct.) 1950.

The data presented seem to indicate that in male and female rats the level of serum acid phosphatase activity is controlled by the adrenal glands, as well as by the testicles in male rats.

Adrenalectomy produced an organism in which the serum acid and alkaline phosphatase and the bone alkaline phosphatase activities, as well as the serum phosphorus, were all at a higher level than in the intact animal.

Testosterone produced little effect.

JACOBSEN, Buffalo.

LOCAL ACTION OF ADRENOCORTICAL STEROIDS ON EPIDERMIS AND CONNECTIVE TISSUE OF SKIN. C. WILLIAM CASTOR and BURTON L. BAKER, Endocrinology **47**:234 (Oct.) 1950.

Hyperactivity of the adrenal cortex induced by treatment of rats with corticotropin results in a general suppression of growth. In the skin, the epidermis becomes thinner, hair stops growing, and the dermal connective tissue assumes a more compact arrangement. These effects appear to be mediated by C-11 oxygenated steroids which are secreted by the adrenal glands. If one of these compounds, cortisone, or an extract of the adrenal cortex is applied directly to the skin, similar changes are induced locally in the epidermis and hair follicles.

Experiments reported in this paper demonstrate that adrenocortical steroids, particularly those of the C-11 oxygenated type, may cause regressive changes in all of the epithelial constituents of rat skin including epidermis, hair follicles, and sebaceous glands. The development of a state of refractoriness to the action of the hormones was demonstrated by the resumption in growth of hair in the area of application when treatment was continued for 180 days.

JACOBSEN, Buffalo.

INFLUENCE OF THIOCARBONAMIDES AND CERTAIN OTHER SULFUR COMPOUNDS ON ALLOXAN DIABETES IN RATS. I. N. ROSENBERG and M. S. RABEN, Endocrinology **47**:251 (Oct.) 1950.

A number of thiocarbonamide and other sulfur compounds were fed to rats with alloxan diabetes of moderate and severe degrees. No essential beneficial effect on the diabetes was found, and no change in insulin sensitivity occurred.

JACOBSEN, Buffalo.

INACTIVATION OF ESTRONE BY RATS IN RELATION TO DIETARY EFFECTS ON LIVER. RAYMOND E. VANDERLINDE and W. W. WESTEFELD, Endocrinology **47**:265 (Oct.) 1950.

Vanderlinde and Westefeld conclude that the results of these experiments are consistent with the concept that protein intake is the critical dietary factor involved in maintaining the estrogen-inactivating system in the liver.

JACOBSEN, Buffalo.

MECHANISMS OF DESOXYCORTICOSTERONE ACTION: RENAL EFFECTS OF WATER-SOLUBLE GLYCOSIDE. D. M. GREEN, A. FARAH, and W. W. KLEMPERER, Endocrinology **47**:281 (Oct.) 1950.

Single doses and continuous infusions of desoxycorticosterone glycoside (DCG) were administered to a series of dogs under various conditions of sodium load. The renal effects were studied in relation to changes in rates of filtration and reabsorption.

The most consistent and striking effect was the increase in water excretion, amounting from 50 to 300% above control values. The rise was due to a decreased tubular reabsorption of water.

The second effect of DCG was a reduction in the urinary sodium concentration.

JACOBSEN, Buffalo.

β-GLUCURONIDASE ACTIVITY IN RAT UTERUS. SAMUEL L. LEONARD and ERNEST KNOBIL, Endocrinology **47**:331 (Nov.) 1950.

Many animal tissues contain an enzyme, β-glucuronidase, which is specific for the hydrolysis of β-glucuronides in vitro. It has been observed that the activity of β-glucuronidase in uterine tissue of ovariectomized mice is significantly less than that of normal animals, and that this activity could be returned to the normal level by the administration of estrogens in physiological doses. These findings led to the supposition that a relationship exists between the activity of uterine β-glucuronidase and the level of estrogenic hormones in the animals studied.

The experiments here reported indicate that uterine β-glucuronidase activity could not be used as an index of physiological changes in estrogen levels during the normal estrous cycle in the rat.

JACOBSEN, Buffalo.

ADRENAL CORTICAL HORMONE LEVELS IN ADRENAL VEIN AND PERIPHERAL BLOOD. K. E. PASCHKIS, A. CANTAROW, A. A. WALKLING, and D. BOYLE, Endocrinology **47**:338 (Nov.) 1950.

There is little information available regarding the rate of secretion of adrenal cortex hormones, their levels in the blood, and their ultimate metabolic rate. This article deals with experiments undertaken to determine the amount of hormone in the blood of the adrenal vein and in the peripheral circulation.

It was found that adrenal cortex hormone levels in the peripheral blood rose following injection of corticotropin or epinephrine, following an "alarming stimulus" including injection of the sympathetic blocking drug, dibenzyl beta chlorethyl amine hydrochloride.

JACOBSEN, Buffalo.

EVALUATION OF AFFERENT NERVOUS IMPULSES IN ADRENAL CORTICAL RESPONSE TO TRAUMA. MARVIN L. GORDON, Endocrinology **47**:347 (Nov.) 1950.

Direct stimulation of a peripheral nerve and exposure of an organism to such purely neurotropic stimuli as sound and light have been shown to produce an increase in adrenal cortex activity. It is the purpose of this investigation to learn to what extent afferent nervous impulses participate in the increased adrenal cortex activity following trauma. The adrenal ascorbic acid concentration was determined, as an index of adrenal cortex activity, following local trauma to innervated and denervated limbs.

It was found that the discharge of adrenal ascorbic acid which normally follows a fracture or mild scald of the leg of normal and adrenal-demedullated female piebald rats was diminished if the traumatized leg had been previously denervated.

JACOBSEN, Buffalo.

EFFECT OF GLUCOSE ON ADRENAL RESPONSE TO ACTH IN HYPOPHYSECTOMIZED RATS. P. CONSTANTINIDES, C. FORTIER, and F. R. SKELTON, Endocrinology **47**:351 (Nov.) 1950.

Ever since the pituitary-adrenal system was recognized as the main humoral regulator of reactions to stress, attempts have been made to influence its function by various procedures. The discovery of agents modifying the function of that system might provide the clinician with effective means of combating diseases resulting from its derangements.

The experiments reported in this paper were aimed at obtaining a broader physiological evaluation of the effect of glucose on the adrenal gland and at determining whether this effect is exerted directly on the cortex or indirectly through the pituitary gland.

It is concluded that the administration of glucose augments the adrenal response to corticotropin (ACTH). Various possible mechanisms and implications of this effect are discussed.

JACOBSEN, Buffalo.

INFLUENCE OF HYPOPHYSECTOMY ON HEMOPOIETIC RESPONSE OF RATS TO LOWERED BAROMETRIC PRESSURES. WILLIAM M. FEIGIN and ALBERT S. GORDON, Endocrinology **47**:364 (Nov.) 1950.

Recent experiments have established a relation between the pituitary gland and hemopoiesis. Thus, anemia, reticulopenia, and bone marrow hypoplasia have now been recognized as features of the posthypophysectomy state in the rat. These blood deficiencies, moreover, can be overcome by anterior-pituitary and other hormones, especially those of thyroidal or androgenic nature.

From the experiments here reported, it is concluded that although the pituitary gland is essential for the erythropoietic response to moderately low pressures (411 mm. Hg), a full effect may be produced independently of this gland at severer levels of anoxia.

JACOBSEN, Buffalo.

ANDROGENIC ACTIVITY OF OVARIAN TRANSPLANTS TO SEMINAL VESICLE OF CASTRATED ADULT MALE RAT. SEYMOUR KATSH, Endocrinology **47**:370 (Nov.) 1950.

From these experiments, it is concluded that an ovarian graft displays androgenic activity when transplanted to the seminal vesicle and that lower thermal surroundings are, therefore, not indispensable for androgen production by such transplants.

JACOBSEN, Buffalo.

MECHANISM OF INSULIN-INDUCED EOSINOPENIA IN RATS. ABRAHAM DURY, Endocrinology **47**:384 (Nov.) 1950.

The eosinopenic effect which follows the injection of insulin in intact rats has been shown to depend upon the presence of the adrenal medulla. It has therefore been suggested that this change in the number of circulating eosinophiles is not an insulin effect but the consequence of an increased liberation of endogenous epinephrine.

JACOBSEN, Buffalo.

CHROMAFFINOMAS IN CHILDREN. EDGAR C. B. BREWER, Arch. argent. pediat. **31**:8 (Jan.-Feb.); 73 (March); and 138 (April) 1949.

This series of articles is devoted to a general review of the subject of chromaffinomas plus a detailed report of a case studied by the author, in a 14-year-old boy with a proved pheochromocytoma of the right adrenal gland. The author states that this is the sixth case to be reported in the total pediatric literature and the third "since the establishment of modern etiopathogenic conception."

PANOS, Galveston, Texas.

TREATMENT OF DIABETIC COMA IN CHILDREN. L. HOSTOMSKÁ and V. KEPKOVÁ, Pediat. listy **5**:79 (No. 2) 1950.

In 1947 the authors revised, on the basis of recent literature and of the personal experience of one of them acquired at Prof. Hagedorns' Clinic in Copenhagen, the treatment of the diabetic coma used until then in the diabetic unit of the Children's Clinic of Prof. Brdlík II in Prague. The authors emphasize the importance of intensive insulin therapy and of sufficient rehydration of the organism by isotonic sodium chloride solution in the first six hours. They explain why they have abandoned, in accordance with the view of other authors, the administration of glucose at the beginning of treatment. They compare the results of their treatment of 10 patients in coma in the years 1947-1949, with the results in 10 patients in similarly severe coma in the years 1945-1947, who were then treated with glucose and insufficient insulin during the first hours. All children treated by the new method recovered, whereas three of the children treated by the older method died and at autopsy nothing but pancreas atrophy could be detected. The duration of diabetic coma has been shortened from 12 to 34 hours to 4 to 15 hours by the new treatment.

FROM THE AUTHORS' SUMMARY.

## Diseases of Muscles, Bones, Joints and Lymph Nodes

HIP DISORDERS IN CHILDREN. LYLE W. RUSSELL, Illinois M. J. **97**:273 (May) 1950.

In establishing a diagnosis of one of the several disorders which may occur in the hips of children, one must combine a careful history and physical examination, roentgenographic and laboratory studies, and often joint aspiration and biopsy. The most important of the diagnostic aids for each of the conditions under consideration, however, may be given in summary as follows: (1) history, physical examination and roentgenograms for all the congenital disorders, coxa plana and epiphysiolysis; (2) laboratory studies and joint aspiration for the infections; (3) roentgenograms and biopsy for the bone tumors.

FROM THE AUTHOR'S SUMMARY.

CONGENITAL STIGMA OF SHOULDERS. ANTONIO GONZALES and MENESES MELENDEZ, Acta pediat. españ. **88**:437 (April) 1950.

The name posterior stigma of the shoulder was given by Ombredanne to the small fossae noted bilaterally and symmetrically at the posterior extremity of the external border of the acromion.

There may be a familial tendency toward this condition, or it may occur spontaneously. When the arms are held downward, the fossae assume an outward and upward position, and with the arms crossed they assume a vertical position with a slight concavity externally. They are 10 to 15 mm. in length and at the base are attached to the superficial surface of the scapulae.

Unlike Ombredanne's cases, in these cases there was no atrophy of the deltoid or other muscles, and no paralysis of the type called "birth paralysis." There was no other pathologic manifestation observed either clinically or roentgenologically.

One patient's father had the same manifestations; and the author wonders whether the concurrence of these fossae with dystrophies, birth injuries, and the like may be incidental rather than in the more serious diseases previously described by Ombredane, Valentin, and Almos.

ALLEN, Santa Fe, N. M.

## Diseases of Eye

PEORIA VISUAL SCREENING PROJECT. CLIFTON S. TURNER and JOSEPH A. POTTOR, Illinois M. J. **97**:151 (March) 1950.

The Peoria Visual Screening Project was initiated in 1948. The plan adopted for the school vision-screening program was developed by a joint committee of ophthalmologists and optometrists and was subsequently approved by the Illinois State Medical Society and the Illinois Optometric Association. A seven-man steering committee appointed to carry out the program consisted of representatives from ophthalmology and optometry, as well as from the Peoria School System, parochial schools, Bradley University, the Illinois Society for the Prevention of Blindness and the city health department.

The Massachusetts Vision Test was the instrument used for screening. It is simply a gross screening method, testing five visual skills.

A total of 12,667 students were screened in the Peoria public and parochial grade schools. The results showed that 17.57% of the students had vision below the minimum standard. The number of children with visual problems gradually increased from 25.1% in the first grade to 53.3% in the eighth grade. Of the 2,226 students below the minimum standard, 20.7% obtained professional care. The chief need uncovered in the program is that for a follow-up of unresponsive parents to urge them to obtain visual care for their children. Public health nurses have ably demonstrated their effectiveness in follow-up procedures.

BARBOUR, Peoria.

## Cutaneous Diseases; Allergy

SOME CASES OF ACRODYNIA. U. GOBBI, Clin. pediat. **31**:664 (Dec.) 1949.

Six cases of acrodynia from the neighborhood of Rimini are reported. In one child at the age of 17 months marked gingivitis developed in the course of the disease, with loss of all his teeth. The use of medicines containing mercury is contraindicated in acrodynia. Vitamin $B_6$ proved quite efficacious in treatment of these patients.

HIGGINS, Boston.

ALLERGIC MANIFESTATIONS DUE TO FEEDING ENCOUNTERED DURING INFANCY. ANGEL CRESPO-SANTILLANA and J. J. LLOPIS REY, Acta pediat. españ. **87**:259 (March) 1950.

In this lengthy article the authors present 15 cases of children under 1 yr. of age who had proved allergies to food. Photographs of the lesions, the skin reactions, and x-ray evidence of pylorospasm and other manifestations of allergy are included. The mechanism of allergy, both congenital and acquired, and the type of family history in which allergies would be likely to be present are discussed. The work on transplacentally acquired allergies is discussed. Also included is a full discussion and bibliography of the various investigations of the antigens, antibodies and their specificity, and the pathogenicity of allergic reactions.

The foods most likely to cause allergies are the animal albumins found in milk, eggs, fish, and meat; the vegetable albumins found in cereals, vegetables and fruits, and certain carbohydrates.

The authors state that transitory pylorospasm of the newborn, melena in the newborn, and the so-called transitory physiological dyspepsia of the newborn are believed to be allergic responses, although other theories of their cause have been propounded earlier. Later the same child may show other allergic responses. In the intestinal tract there may be pylorospasm, allergic gastritis, spasm of the colon, allergic enteritis, and colitis.

Under eczema, the authors discuss the clinical characteristics which appear before the second month and never after the sixth month of life and compare the histologic appearance of the skin of the normal child with that of the child with eczema.

Urticaria, both diffuse and papular, is described as to etiology, pathology, and its association with other entities of an allergic nature, with especial emphasis on the association of alimentary reactions and skin reactions. The papular type is often associated with infections of a virus type.

Angioneurotic edema, with its dramatic symptomatology, is also discussed, as is the Schönlein-Henoch type of purpura.

Rarer manifestations are rhinitis and fever, which may be the reaction a child gives to the ingestion of allergic foods. These symptoms are usually noted to follow the inhalation of allergens rather than the ingestion of foods.

The authors give minute detail regarding necessary diagnostic procedures. They include a sample sheet used in securing a very detailed family and personal history, and they list the symptoms that may be due to an allergy as distinguished from those that are proof of an allergic reaction.

The various tests, including the Prausnitz-Küstner, are fully explained and evaluated. Technical tests for recovery of antibodies and for determination of microprecipitins in the blood stream and the old clinical test of the "elimination diet" are described.

Under the heading of treatment, the psychotherapy of the family, prophylaxis, specific treatment, nonspecific treatment, and symptomatic treatment are discussed in detail.

Dietary-substitution treatment is discussed very thoroughly, with emphasis on an adequate high-vitamin diet despite the limitations imposed by the allergies.

Under symptomatic treatment, the authors discuss various lotions and unguents which have been popular and useful. Most of them are familiar to English-speaking readers. Suggestions for the use of epinephrine, ephedrine, and calcium, and a rather detailed discussion of the various antihistamines are also included. The last-named drugs are for relief of symptoms only and are not to be given indiscriminately. Sedatives should not be withheld if symptoms call for them.

In the last portion of the paper the various manifestations of allergy are discussed with reference to treatment for each kind, varying from the use of powder on the urticarial blebs to the rather complicated treatment for Schönlein-Henoch purpura.

ALLEN, Santa Fe, N. M.

LOCAL PENICILLIN INJECTIONS IN CASES OF PARONYCHIA. GERHART MEIER-STAUFFER, Wien. klin. Wchnschr. **62**:318 (May 5) 1950.

In children with paronychia 600 units of penicillin was injected all around the diseased area with the patient under short slight ether anesthesia. In 86% the causative micro-organisms were penicillin-sensitive.

AMBERG, Rochester, Minn.

TREATMENT OF LEINER'S DESQUAMATIVE ERYTHRODERMA WITH DESOXYCORTICOSTERONE ACETATE AND POTASSIUM. L. BARTA and E. FARKAS, Pediat. danub. **6**:231 (Oct.-Dec.) 1949.

Patients with Leiner's disease in both the acute and the chronic stage responded surprisingly well to treatment with desoxycorticosterone acetate and potassium. Although edema formation is usually enhanced by desoxycorticosterone acetate, after the simultaneous administration of small doses of potassium, disappearance of edema was noted. It is assumed that the ceasing of some cellular dysfunction may explain the paradoxical effect.

As these observations are almost entirely clinical, no conclusions are drawn. Still, it is recommended that therapy with desoxycorticosterone acetate and potassium in both the acute and the chronic cases of Leiner's disease be tried, but only under close institutional supervision.

FROM THE AUTHORS' SUMMARY.

ABDOMINAL ANAPHYLACTOID PURPURA IN INFANT. J. KAMARAS, Paediat. danub. **6**:266 (Oct.-Dec.) 1949.

The abdominal form of anaphylactoid purpura was observed in an 11-month-old infant. In the first week of the disease, hemorrhages could be provoked by intracutaneous injection of protein. After a week, when no more spontaneous hemorrhages occurred, provocation was unsuccessful. It follows that the antigen which originally elicited the hemorrhages differed

from the proteins of both tuberculin and milk. It is supposed that it might have been some endogenous antigen that had been developed in connection with repeated attacks of pharyngitis.

In the presence of the original antigen, every kind of protein administered parenterally acted as an antigen. After the patient's recovery, the endogenous antigen disappeared and then foreign proteins had no more antigenic effects.

FROM THE AUTHOR'S SUMMARY.

β HEMOLYTIC STREPTOCOCCI IN THE DISEASE GROUPS ECZEMA INFANTUM-PRURIGO. ANJA HELVE, NILS OKER-BLOM, and RISTO PÄTIÄLÄ, Acta pædiat. **39**:140, 1950.

A great number of hemolytic streptococci were found in the wards in which eczematous children were nursed in the Children's Clinic of the University of Helsinki. Nose, throat, and skin swabbings obtained from such children of varying ages yielded numerous streptococci upon culture. The antistreptolysin titer of these children was usually low, as were the sugar-tolerance values at the manifest stage of the disease.

FROM THE AUTHORS' SUMMARY.

## Surgery and Orthopedics

ANESTHESIA FOR OPERATIONS ON THE HEART AND GREAT VESSELS. G. A. LIGHT, H. M. LIVINGSTONE, and W. E. ADAMS, Arch. Surg. **60**:42 (Jan.) 1950.

The authors surveyed 58 cases in which 60 intrathoracic operations on the heart or great vessels have been performed, and the results are summarized. There were four postoperative deaths and two deaths in the operating room, making a total mortality rate of 10%. The general management of the patient is discussed in detail. Special emphasis is placed upon the anesthesia and the reasons for using a particular type of anesthetic. Ether was chosen as the chief anesthetic component for the majority of patients. Ether, after induction with vinyl ether, ethylene-oxygen, or nitrous oxide-oxygen, was administered during the maintenance period with oxygen or oxygen with a gaseous anesthetic agent if the patient's oxygen requirement permitted it, and with positive pressure when the chest was open. Postoperatively oxygen is administered for at least 24 hr. or longer. A brief review of the management of patients in the diagnostic procedure of cardiac catheterization is also presented.

KAISER, Rochester, N. Y.

MEDICAL CARE IN MAJOR PEDIATRIC SURGERY. J. ROBERT BOWMAN, South. M. J. **43**:720 (Aug.) 1950.

Bowman gives a very good review of preoperative and postoperative care in infants and children, with detailed suggestions regarding the use of blood, plasma, and albumin as well as for the administration of other fluids and electrolytes. (The author does not mention the danger of hepatitis when pooled plasma is used.)

Problems in anesthesia are discussed, including some statements about the controversial subjects of preoperative medication. Some of the problems of postoperative care and means of meeting them are given. The author points out that infants and children who receive adequate preoperative and postoperative medical care and who are operated upon with due respect for young, tender tissues tolerate major surgery amazingly well.

LOGAN, Rochester, Minn.

PHYSIOLOGICAL FACTORS OF SIGNIFICANCE IN PEDIATRIC ANESTHESIA. C. R. STEPHEN, Canad. M. A. J. **63**:109 (Aug.) 1950.

Attention is called to various physiological factors which must be considered in pediatric anesthesia. The author states that only small deviations from normal can be tolerated for any length of time. He calls attention to the insidious onset of hypoxia, with few early objective signs, and to the serious changes it may initiate not only in the cerebral cortex but also in the biochemistry of the blood and other tissues. Reflex neurogenic stimuli created by the surgeon should be recognized and treated by the anesthetist. Thoracic surgery presents a problem of cardiovascular reflexes, in addition to altered respiratory pressure relations. The physiological effect of therapeutic drugs as well as anesthetics must also be of constant concern to the anesthetist. The aim of the anesthetist must be to produce the desired result for the surgeon with as little physiological disturbance of the patient as possible.

MCGUIGAN, Evanston, Ill.

CONTINUOUS "MILIEU" BATH AND ALKALI PLASMA TRANSFUSION IN THE TREATMENT OF BURN DISEASE. R. BUCHER, Schweiz. med. Wchnschr. **80**:633 (June 17) 1950.

After gentle débridement, further cleansing of the burned areas is done in a continuous bath of isotonic and isoionic Ringer's solution without calcium. Considerable stress is laid on the temperature of the bath, which should be between 37.2 and 38 C. (never exceeding 38 C.). Alkali plasma (containing 5% sodium bicarbonate) is given intravenously in the amount of 50 ml. three or four times in 24 hours, and also 200 to 300 ml. of citrated plasma. For further detail and the theoretical consideration, the paper is to be consulted.

AMBERG, Rochester, Minn.

## Teeth and Dentistry

FACIAL CLEFTS AND THEIR SURGICAL MANAGEMENT IN VIEW OF RECENT RESEARCH. W. B. SLAUGHTER and A. G. BRODIE, Plast. & Reconstruct. Surg. **4**:311, 1949.

On the basis of the findings of more recent research on the relation of facial clefts in the embryo to later growth of the face, Slaughter and Brodie present a theory, supported also by their own surgical experience, that the older method of early correction of the bony defect in cases of cleft palate and cleft lip is responsible for later deformity. By the means of roentgenograms and the use of dyes, a study of the postnasal growth of the maxilla has shown that this change is the determining factor in the final positioning of the parts of the maxilla and of the form of the mature face. There is general growth of the face until about 5 yr. of age. Thereafter, facial growth continues in the sutures and synchondroses of the skull, by proliferation of cartilage. This growth about the maxilla controls the final position of the parts of the face and is consequently concerned in the occurrence of cleft palate and cleft lip. The authors are of the opinion that injury from early operation on the bony margins of the maxilla, where later postnatal growth occurs, may destroy this potentiality, with consequent lack of normal relations of these parts. They have shown by their own experience that early corrections of only the soft parts averts disturbance of normal growth of the bone, leaving the action of the muscles and skin to mold the bony relations of the cleft palate and lip. The text is well illustrated by drawings and photographs, and 16 references to related literature are given.

SELTZER, Philadelphia [ARCH. OTOLARYNG.].

## Miscellaneous

EFFECTS OF IODIDES AND OTHER HALIDES GIVEN WITH THIOURACIL. J. K. W. FERGUSON and E. A. SELLERS, J. Pharmacol. & Exper. Therap. **97**:177 (Oct.) 1949.

Concurrent administration of iodide and thiouracil or propylthiouracil for two to six weeks results in thyroid glands which are 20 to 30% lighter than those produced by the administration of thiouracil or propylthiouracil alone. Iodide does not decrease the effectiveness of the goitrogenic drugs in lowering the metabolic rate. Consequently, its antigoitrogenic action cannot be attributed to an increase in the supply of available thyroid hormone.

The thyroid follicles of the rats receiving iodide with thiouracil contain more colloid and show less hyperplasia. The effect of the iodide seems to be best described as antithyrotropic in some sense.

PILCHER, Cleveland.

INFLUENCE OF DIPHENHYDRAMINE-HCL (BENADRYL®) ON APOMORPHINE-INDUCED EMESIS IN DOGS. GRAHAM CHEN and CHARLES R. ENSOR, J. Pharmacol. & Exper. Therap. **98**:245 (March) 1950.

For several years the authors' laboratory has been studying the antiemetic actions of apomorphine-induced vomiting in dogs, with the hope that "such agents may possibly be of value in the management of emesis in man." Diphenhydramine, by mouth, lessened vomiting, salivation, and the intensity and duration of retching. Dimenhydrinate (dramamine®) was also similarly effective. Phenobarbital and atropine were effective only in hypnotic doses. As the authors suggest, these drugs could well be tried clinically.

PILCHER, Cleveland.

SIMPLIFICATION OF DRUG DOSAGE CALCULATION BY APPLICATION OF THE SURFACE AREA PRINCIPLE. JOHN D. CRAWFORD, MARY E. TERRY, and G. MARGARET ROURKE, Pediatrics **5**:783 (May) 1950.

The pediatrician customarily bases drug dosage on a unit of body mass, while the practitioner dealing largely with adults generally uses a single dose level of a given drug for all his patients. The inaccuracies of this system are quickly apparent, particularly to the pediatrician, who sees patients varying widely in size. A straight-line relation was found for two drugs, sulfadiazine and acetylsalicylic acid, between dosage for each unit of patient surface area and concentration of the drug in body fluids. This suggested that prescriptions of drug dosage on the basis of a unit of surface area rather than a unit of body mass might provide a means of achieving greater uniformity of pharmacologic effect in patients of differing size. A clinical trial of this method of calculation applied to a wide variety of drugs has indicated that it results in a high degree of accuracy with respect to dosage. It also represents a simplification in prescription methods, since one can easily calculate by this method the dosage for a patient of any size, if one knows the standard adult or infant dose.

FROM THE AUTHORS' SUMMARY.

REDUCED ABSORPTION OF AUREOMYCIN CAUSED BY ALUMINUM HYDROXIDE GEL (AMPHOJEL). BURTON A. WAISBREN and G. S. HUECKEL, Proc. Soc. Exper. Biol. & Med. **73**:73 (Jan.) 1950.

Because aureomycin in some instances produces gastric distress, nausea, and vomiting, aluminum hydroxide gel (amphojel®) has been given to counteract these effects. The serum values for aureomycin were determined on five hospitalized patients and six normal male subjects. Aureomycin was administered for three consecutive days, and during the ensuing three days aureomycin was given together with aluminum hydroxide gel. In four of the patients there was a fall in the serum level of the aureomycin within a 24-hr. period after the aluminum hydroxide gel had been taken together with the aureomycin. Aureomycin administered alone produced levels which averaged 5.9 mg. per milliliter, with a range of 1.2 to 10.2 mg. per milliliter. After 48 hr. of the combined medication all serum levels were less than 1 mg. per milliliter. A fifth patient did maintain a level of 5 mg. per milliliter in spite of the aluminum hydroxide gel. The authors conclude that these two drugs should not be used together.

HANSEN, Galveston, Texas.

PREGNANCY DIET IN RELATION TO CHILD HEALTH. MUKTA SEN, Indian J. Pediat. **18**:65 (April) 1950.

The importance of adequate diet for the pregnant woman is stressed. The author feels that deficient diet in the mother results not only in increased incidence of prematurity, fetal anemia, and lower average birth weight but also in increased incidence of illness in older infants.

McGUIGAN, Evanston, Ill.

TREATMENT OF INFANTS AND SMALL CHILDREN IN THE HOSPITAL WARD SERVICES. P. ROHMER, Lattante **21**:65 (Feb.) 1950.

The routine policies in vogue at the pediatric clinic at Strasbourg are discussed, especially the handling and prevention of contagious diseases, infectious diarrhea, upper respiratory tract infections, and the premature infant.

HIGGINS, Boston.

# News and Comment

## ANNOUNCEMENTS

**Postgraduate Course in Pediatric Allergy.**—A postgraduate course in pediatric allergy will be given under the direction of Dr. Bret Ratner, Professor of Clinical Pediatrics and Associate Professor of Immunology, and members of those departments, at New York Medical College, Flower and Fifth Avenue Hospitals, on Wednesdays from Nov. 7, 1951, through May 28, 1952, in all, 30 sessions. The fee will be $300. The course consists in lecture-seminars, laboratory, clinical procedures, clinic work, ward rounds, and animal experimentations. Lecture-seminars cover the basic principles, diagnosis and treatment of allergy in children, and applied immunology. Applicants must be certified in pediatrics or have the requirements for certification. The group is limited. Applications should be made to the Dean, New York Medical College, 106th St. and Fifth Ave., New York 29.

**Research Fellowship in Pediatric Allergy.**—A research fellowship in pediatric allergy under the direction of Dr. Bret Ratner is available in the Departments of Pediatrics and Immunology at New York Medical College, 106th St. and Fifth Ave., New York 29. The fellowship starts Jan. 1, 1952. It runs from one to two years and will consist in intensive training in immunology and animal research pertaining to the field of hypersensitiveness, intensive study of allergic children, which will include skin testing, laboratory work, clinical follow-up, and clinical research. Applicants must be certified in pediatrics or have the requirements for certification. Applicants who have had previous training in chemistry and/or immunology and who are desirous of a research career will have preference.

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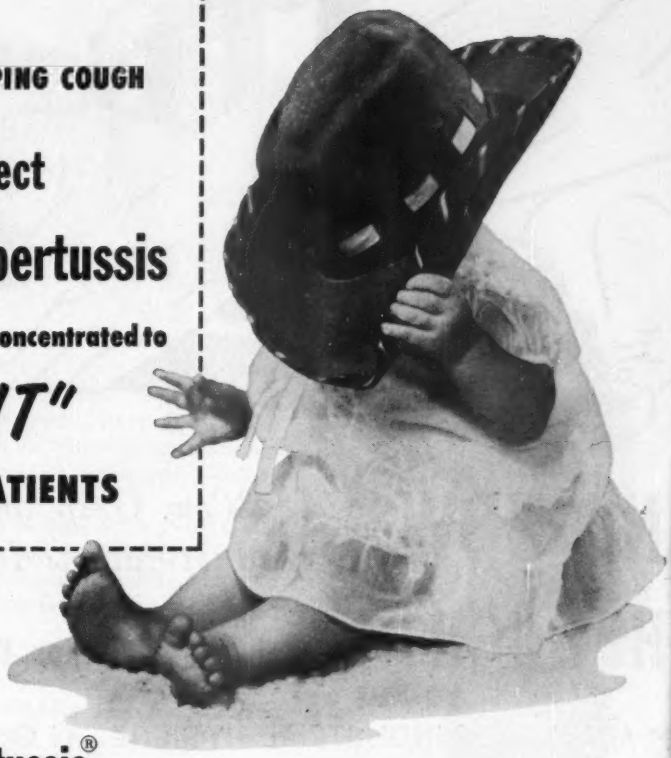

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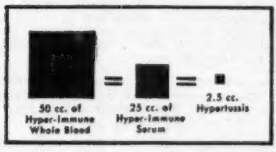


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*Clein, N. W.: Cow's Milk Allergy in Infants, *Annals of Allergy*, March-April, 1951.

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'Dexin' is composed of 75% dextrins and 24% maltose. The small amount of maltose is quickly assimilated. The dextrins are not fermented by the usual intestinal bacteria. This *does* make a difference in comfort to the baby.

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*Tins of 12 oz. and 3 lbs.*

*6 level-packed tablespoonfuls of 'Dexin' = 1 oz. = 115 calories.*

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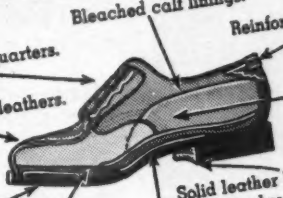
# FLEET-AIR Correctives . . .



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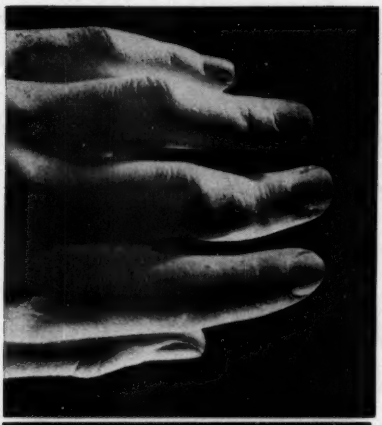

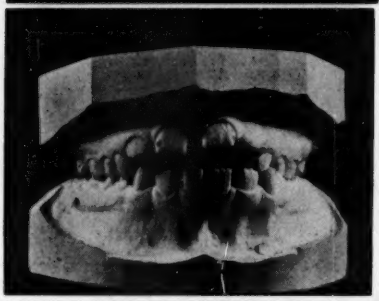

# Untoward Results

## OF PERSISTENT FINGER-SUCKING

**MODEL**

is 7½ years old. Unretouched photographs and description from a leading children's dental clinic.

**Hand**—sucked two middle fingers left hand since age 4. Note deformity caused.

**Mouth**—case shows deformed shape of mouth and displacement of teeth due to pressure of fingers.

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*--prescribe--* THUM TRADE MARK

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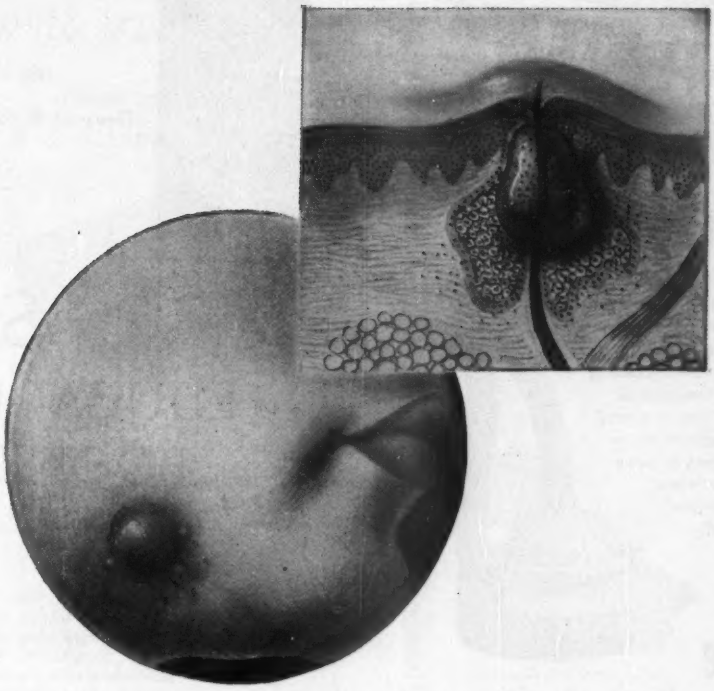

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*Wright, L. T., et al: Antibiotics and Chemotherapy 1:165 (June) 1951.*

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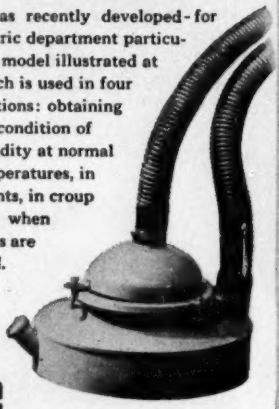

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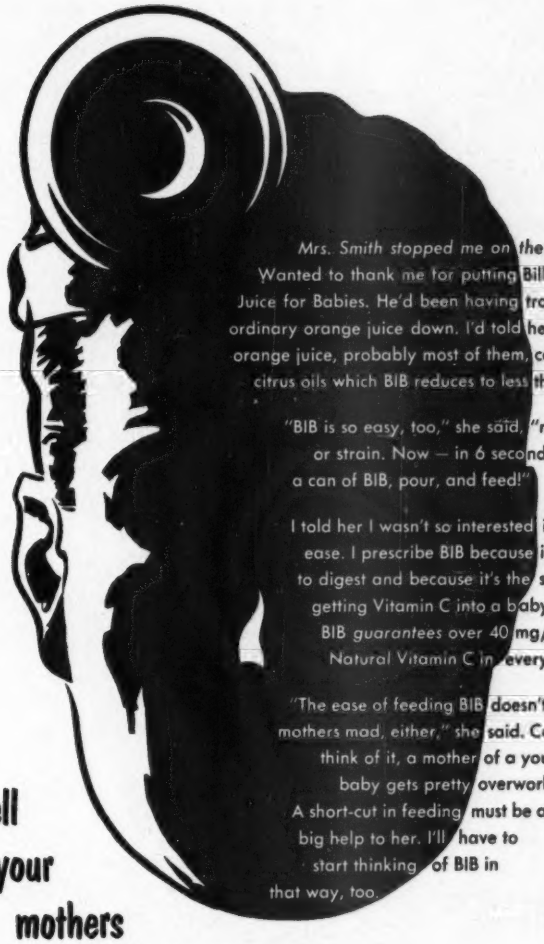

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